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DISEASES OF THE KIDNEY

&c.

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DIABETES

BY

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PREFACE.

THIS little treatise is in part fulfilment of an intention I expressed in introducing my book on Albuminuria, now seven years ago. It was my design to treat not only of albuminuria, but of all the more important disorders which either belong to the kidneys or are mainly declared by the urine. The project now approaches completion. I propose to issue the work in three parts, to form ultimately one volume. In arranging the sections I have made the convenience of purchasers a leading consideration, taking for the first and second parts, both of which will be complete in themselves, subjects which are practically isolated; so that a person interested in one of these subjects only may obtain what refers to it unburdened by any other matter, while the possessor of one of the earlier subdivisions who is not led by his estimation of the performance to desire more of it will find what he has complete without further addition.

Diabetes, now published, is the first instalment; the next will be, in fact, a second edition of the treatise on Albuminuria, which has been long out of print; the third and concluding part will deal with the organic renal changes which do not come under the heading of albuminuria: abscess, embolism, and thrombosis, growths and

cysts, renal calculi, their antecedents and results, and finally with some conditions, for the most part symptoms rather than diseases, which since they may be dependent on several morbid states are most conveniently considered subsequently to all. Among these may be mentioned suppression of urine and hæmaturia. And, as conceivably related to the discharge of blood with the urine, the disorder which is characterized by the admixture with it of chyle will follow.

The second and third parts will quickly succeed the first; the second has been already before the public, and will shortly reappear with some necessary additions; the third is nearly ready for the press, and will shortly follow the second.

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DIABETES MELLITUS.

INTRODUCTION.

In approaching the subject of Diabetes Mellitus, or Diabetes, for the single word is by common consent limited to the disorder to which the term *mellitus* is applicable, if it be necessary to commence with its definition, I would venture to say—

Diabetes is a disease of the nervous system characterised by the secretion of saccharine urine.

For this description of a disease which has been regarded from other points of view, and often vaguely designated as functional, my warrant will be found in what is to follow.

Excess of urine, thirst, and wasting appear to have been recognised as the symptoms of a disease to which the term diabetes was applied, even as far back as the time of Aretæus. The leading peculiarity of the urine, however, escaped notice or mention until it was made known about the year 1674, by the learned and acute Thomas Willis,[1] not the Rev. Dr. Willis, the stern physician of George III., but he who classified the cranial nerves, and gave his name to the arterial circle at the base of the brain. In an account of 'the diabetes,' which was then commonly called, as he tells us, '*hydrops ad matulam*,'[2] he dwells upon the sweetness of the urine

[1] Thomas Willis died in 1675.

[2] 'On the Operations of Medicines in Man's Body,' sec. iv. chap. iii.

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as if mixed with sugar or honey, and describes with much accuracy of observation the causes and symptoms of the disease. He refers it to 'the guzzling of strong wines,' and to mental causes, 'sadness, or long sorrow,' and holds that the nervous juices play an essential part in its origination. Wise in his generation, he regarded the distemper as more immediately 'of the blood than of the reins,' connected with a loosening of its temper and discharge of the watery and saline particles.[1]

Sydenham,[2] who makes no reference to the cardinal observation of his senior, regards the complaint from a similar point of view, and describes its leading symptoms with his accustomed force and brevity.

'The juices of the blood make a way out through the urinary passages, in an unconcocted form. Hence the strength gradually lessens, and the body weakens, its substance being, as it were, pumped out through the common sink of the bladder. Then there are thirst, heat of the viscera, swelling of the legs and hips, and the frequent expectoration of a viscid and frothy saliva.'

It is not necessary to follow the subsequent steps by which diabetic sugar was isolated and identified with that of the grape, or to review the various hypotheses as to the nature of the disease which our present knowledge enables us to discard.

The term functional, which is usually attached to diseases of which the essential lesions are undiscovered or not generally known, has been commonly applied to diabetes; which in this view is perverted action without structural change. But irrespective of observation, it would be to me incredible that this intractable and destructive disease, persistent as it is under every alteration of external circumstances, so clearly belonging to the body and not to its surroundings, should be independent of organic alteration. But so it has been for the most part regarded.

[1] 'Processus Integri,' ch. xxxvii.

[2] 'Translation by the Sydenham Society,' vol. ii. p. 283.

The deficient action of oxygen has been supposed to lie at the bottom of the disturbance; but we cannot trace the disease to dyspnœa or cyanosis, we cannot learn that the diabetic receives in any way less oxygen than his fellow, nor can we understand how it is if his organs be natural that they cannot apply it naturally. The suboxidation theory of diabetes is an example of the somewhat inconsiderate manner in which complicated organic processes are divested of organic influence and cramped into the ideal simplicity of chemical equations. All chemical laws hold good in the body as out of it, and probably extend with the universe, but in applying them to the living body it is necessary to consider the action of the body itself. The body is not a passive receptacle, within which substances act upon each other without interruption or assistance, but a complicated and active mechanism, which executes many combinations and re-arrangements of which the materials would not otherwise have been capable. Thus the body is not a test glass whose contents are unaffected except by each other, nor a retort of which we know the product when we know the supply, but rather a loom,—although nothing can come out of it but what has first been put in, yet the shape in which it issues is given to it by active and variable machinery, so that the same fibre may with different adjustment be manufactured into diverse fabrics. So perhaps in the animal frame the same staple, to take a hypothetical case, may, according to the adjustment of the machinery, be woven into one breadth as albumen, or into two, one being urea and the other sugar.

Before proceeding to the nature and symptoms of the disease, it will be necessary to state in brief the present condition of our knowledge with regard to the formation of sugar in the body. Doubts which still prevail will make it necessary for me in this compilation, to give not a mere abstract of results, but a somewhat detailed statement of concurring and conflicting views.

CHAPTER I.

PHYSIOLOGY OF GLYCOGENESIS AND GLYCOSURIA.

ON THE FORMATION OF SUGAR IN THE BODY.

IT used to be thought that the making of sugar was properly a vegetable function, and did not take place in the animal save as the result of disease. This limitation, however, is obviously too strict, since, as has been observed, sugar is a necessary constituent of the milk even of the carnivora. With animals who eat only flesh, it is evident that such sugar as they secrete must have been developed by their own bodies since none enters from without.

With the researches of Claude Bernard a new epoch commences.

Discovery of sugar in the liver.

In the year 1848, Bernard and Barreswil astonished the Academy of Sciences by the display of some alcohol made from sugar extracted from the liver; and they inferred that sugar was developed in this organ since it was found there in animals dieted solely on flesh. Further experiments, some of which I was by his courtesy enabled to witness, completed Bernard's famous doctrine of animal glycogenesis. He found sugar abundantly in the blood leaving the liver by the hepatic vein, though there was none in the blood on its way to it by the portal vein. The sugar, however, was not at once formed as such, but passed through an amyloid stage. A peculiar animal starch or glycogen was produced in the liver, even though the diet had been restricted to flesh. This product was extremely unstable, continually passing into sugar, both during life and after death, by virtue of a kind of fermentation set up by the contact of blood; blood, saliva, or almost any animal fluid being sufficient to effect the transformation.

I may relate the following experiment performed by Bernard

[1] 'Comptes Rendus,' 1848, p. 514.

in illustration of the rapid transformation of the animal starch into sugar.

A rabbit was killed. The liver was quickly taken out, a canula put in the portal vein and a stream of water directed through the circulation of the organ. The fluid passing from the hepatic vein was collected in three separate vessels. The first issue, almost pure blood, gave evidence in reduction of copper of abundant sugar; the second issue, blood largely diluted, contained less sugar; the last issue, almost pure water, appeared to contain none. The exsanguine liver was now tested and found to contain no sugar. A portion of the liver thus washed free from sugar was now mixed with saliva and warmed; it gave decided reaction. A fresh conversion of the amyloid matter had been determined by the admixture.

Production of sugar from hepatic starch.

A similar reproduction of sugar in a liver which had been washed free from it, was shown by other experiments to take place under the influence of time, aided only by such fermentive action as belonged to the substance of the liver itself.

Such experiments illustrate not only the translation of the amyloid matter into sugar, but also the readiness with which the sugar is removed from the liver by a current in the blood vessels. The indiffusible starchy matter may accumulate, but the diffusible sugar necessarily makes its way into the circulation. The starch is inert, indiffusible, and capable of accumulation or storage; the sugar is an active principle of nutrition, which traverses membranes with facility, and is either at once used in the body or quickly makes its escape from it.

This leads to a consideration of the views which have been advanced by Dr. Pavy. This physiologist, though he does not question the accuracy of Bernard's experiments, differs in one respect from his conclusion. Admitting, with all other experimenters, the formation of starch in the liver, Dr. Pavy considers that its subsequent transformation into sugar does not take place during life, but is simply the result of post-mortem change. He shows that blood removed from the right ventricle during life by means of a catheter introduced by one of the veins, contains a very small proportion of sugar, though he allows that it is not absolutely devoid of that substance.

Thought by Pavy to be a post-mortem change.

He asserts, as the result of numerous experiments, that the blood of every part of the circulating system presents in respect of sugar as nearly as possible the same behaviour. And he shows

that if instantly upon its removal from the body, a piece of liver be either frozen or subjected to the action of boiling water, by either of which steps fermentive changes are arrested, the tissue, instead of giving evidence of sugar in abundance, displays only a trace, but still a trace. His experiments have been repeated and varied by Dr. M'Donnell, who adopts Dr. Pavy's view that the formation of sugar is a post-mortem phenomenon. He found, as did Dr. Pavy, that a portion of liver frozen immediately upon removal from the body gave 'an indication of sugar barely perceptible,' while a part which was left to itself for twenty minutes became abundantly saccharine.

Such experiments prove what is indisputable, namely, that the change of glycogen into sugar may take place after death; that it is not a vital but a chemical process. They fail to prove that the conversion does not occur during life, though they show that during life the sugar does not accumulate, being possibly washed away by the circulation nearly as fast as formed.

Bernard [1] had already shown that the exposure of a living frog to cold caused sugar to disappear from its liver; while this product increased under the influence of heat. He thence inferred that the activity of the glycogenic function varied with temperature.

Absence of hepatic sugar after death by freezing.

Dr. M'Donnell, refining upon Bernard's result, found that the disappearance of sugar was influenced by the rate of freezing. The liver of an animal slowly frozen to death displayed no trace of sugar; while that of another frozen rapidly was saccharine. He explains the difference by the occurrence of struggling with rapid freezing,[2] which with the slow approach of cold was absent. Violent movement, according to Dr. Pavy, dislodges the amyloid matter, and causes its admixture with blood and consequent conversion into sugar. Another explanation of the difference may however be hypothetically offered. When death from cold is protracted there is time for the complete consumption of the sugar in the maintenance of vital heat; a process which the rapid advent of death with quick freezing may leave incomplete.

The increased combustion of the body under the influence of cold forbids us to accept animals killed by it as presenting a natural condition with regard to the presence of this convertible and consumable substance, or to conclude that the absence of sugar from the liver, in such circumstances, is the condition of health.

[1] 'Comptes Rendus,' March 1857.

[2] R. M'Donnell, M.D., 'On the Functions of the Liver,' p. 6.

And other considerations, some of which have been urged by Dr. Harley, militate against the views maintained by Pavy and M'Donnell.

Sugar in arterial blood.

Sugar is a normal constituent of the arterial blood even of flesh-fed animals. Dr. Harley [1] fed a dog for four days solely on boiled flesh, perfectly devoid of sugar. Blood from the femoral artery was then discharged directly into boiled acidulated water, and sugar detected in the solution. This and other similar experiments prove beyond doubt that the manufacture of sugar is conducted and completed in the living body, since it is found where none has been introduced and while as yet there has been practically no interval for post-mortem decomposition. Tracing the sugar to its origin there appears to be no doubt that it is derived by the transformation during life of glycogen of which the liver is the chief source. Whether all the glycogen is thus converted, and if not in what manner the rest is applied, are questions still *sub judice*. The observation of Bernard, that in flesh-fed animals hepatic venous blood contains sugar while portal does not, has received abundant confirmation. I may quote the observations of Schmidt of Dorpat made upon dogs.[2]

	Percentage of Sugar in	
	Portal Vein.	Hepatic Vein.
1. On animal diet . . .	0·00	0·93
2. " . . .	0·00	0·99
3. Fasting for two days . .	0·00	0·51

These observations, and they do not stand alone, are irreconcileable with Dr. Pavy's [3] belief that there is nothing special in the blood which escapes from the liver. Such experiments prove that the blood has obtained in the liver either sugar or its antecedent, and the only question is when the glycogen reached the saccharine stage.

Not in in hepatic blood.

Professor Flint detected sugar in the hepatic vein of a dog within a minute of death, and Professor Lusk [4] found that in dogs the blood obtained from the right side of the heart by catheterisation during life contained from twice to four times as much sugar as that in the blood of the jugular vein.

[1] 'The Urine and its Derangements,' p. 224.

[2] 'Comptes Rendus,' vol. xlix. p. 63.

[3] Pavy on 'Diabetes,' ed. 2nd, p. 68.

[4] 'New York Medical Journal,' July 1870.

Sugar probably made in liver during life.

Dalton[1] has recently made some experiments which go far towards placing beyond further question the belief that the liver makes sugar not only after death but during life. He attributes the failure of some observers to find sugar immediately after death to the small quantity of liver tissue employed, and the imperfect application of the copper test. His subjects were dogs previously fed upon bullock's heart, a kind of muscle which contains no glycogen. By rapidly slicing a piece from the living liver and passing it through a mill directly into alcohol or boiling water, he found that he could, in a space of time which varied from 3 to 15 seconds, translate the living tissue into a pulp so mixed with one of these fluids as to be secured from catalytic or fermentive action. A solution thence obtained, clarified by animal charcoal, never failed to show the presence of sugar. The amount averaged $2\frac{1}{2}$ parts to 1000 of liver substance. The spleen subjected to the same process gave no trace of sugar, showing that this substance was not derived from the common arterial blood, but was an essential hepatic product.

Accepting, therefore, the view of Bernard that sugar is formed during life, while at the same time there is no proof that sugar is the only or even the chief issue of the hepatic glycogen, I will proceed to add a few particulars which may help to render less incomplete this sketch of the physiological relations of sugar.

Glycogen can be extracted by water from the healthy liver of almost any animal, forming a milky solution from which it can be thrown down as a white precipitate by alcohol, or better, by glacial acetic acid. It is formed probably in the hepatic cells, certainly external to the blood vessels, since it remains after these channels have been completely emptied by washing. It gives a reddish colour with iodine, and more nearly resembles dextrin than any other vegetable product. It must not be confused with the nitrogenous deposit of lardaceous disease to which the term *amyloid* has been unhappily applied.

Glycogen.

The composition of glycogen is represented by the formula $C_6H_{10}O_5$—identical with that of starch and dextrin. The substance might therefore be properly called amyloid but for the confusion which is inseparable from the term.

The contact of blood, saliva, pancreatic juice, or of the hepatic

[1] Dalton's 'Treatise on Human Physiology,' ed. 5th, 1871, p. 193.

tissue itself, is sufficient to set up a sort of fermentation by which it becomes transformed into sugar. Glycogen does not belong solely to the liver, though this gland is its chief source. In early fœtal life it exists in the placenta and amnion and in many of the embryonic tissues, particularly the muscles and the lungs. The large amount in which it exists would lead to the belief that it plays an important part in connection with development. It has been stated to exist in the white blood corpuscle. With this exception, however, it is found in adult animals only in the liver and muscular tissues. The liver is practically its great source. In this organ it varies according to the quantity, kind, and time of food and the general health of the animal. It appears to attain its maximum in the lower animals generally about six hours after a full meal. Under the influence of disease or starvation it may be totally absent. With the kind of food also it varies largely, attaining its maximum with starch and sugar; more scantily produced from albumen and fibrine; while it falls to its minimum under gelatin and oil.

Its relation to urea.

With regard to the elaboration of glycogen upon a purely nitrogenous diet, Professor Haughton has ingeniously, and with much probability,[1] suggested that the nitrogenous element of nutrition is broken in the liver into two fragments, the one being glycogen, the other urea. The elements of albumen nearly supply the elements of these two substances, the nitrogen going to the urea, the hydrogen and carbon chiefly to the glycogen. Taking protein, for simplicity, it can easily be shown that with the addition of water, carbonic acid and oxygen, the division of its constituents can be theoretically accomplished. Slightly to modify an equation given by Professor Haughton, it appears that 2 Protein + 11 Water + 4 Carbonic Acid + 3 Oxygen = 4 Urea + 6 Glycogen.

$$\overset{\text{Protein.}}{2\,(C_{18}\,H_{27}\,N_4\,O_6)} + 11\,(H_2\,O) + 4\,(C\,O_2) + 3O$$

$$= \overset{\text{Urea.}}{4\,(C\,H_4\,N_2\,O)} + \overset{\text{Glycogen.}}{6\,(C_6\,H_{10}\,O_5)}.$$

Urea is, if the researches of Cyon are to be accepted, largely produced in the liver; and the fact that in diabetic urine the sugar and urea usually increase and diminish together, warrants the belief that they have a common and simultaneous origin.

[1] Professor Haughton, 'On Diabetes Mellitus,' 'Dublin Quarterly Journal,' November 1861, p. 269.

On the Influence of Food upon the Production of Glycogen.

Connected as the hepatic glycogen is with the source of diabetic sugar, it becomes of the highest practical importance to ascertain how the amount of this material varies with different kinds of food.

Dr. Pavy[1] made a number of experiments bearing upon this question, the subjects of which were dogs and rabbits.

With dogs fed solely upon animal food, he found the proportion of glycogen in the liver, taking the average of seven experiments, was 7·19 per cent. Upon vegetable food, potatoes with barley meal or bread, the average percentage of glycogen in three livers proved to be 17·23; and not only was the proportion of glycogen in the liver thus increased, but the liver was almost exactly doubled in its weight relatively to that of the animal. Thus the quantity of glycogen which the dog forms upon meat is more than quadrupled by a diet of potatoes and grain.

Upon animal food mixed with sugar, results similar to those obtained from starch were produced. With four dogs, the glycogen gave an average of 14·5 per cent.; the livers being increased in size as under farinaceous food, with loss of consistence and colour. The urine was generally saccharine.

With rabbits, the same observer found similar results. With two of these animals killed fasting, the livers respectively yielded 1·3 and 1·4 per cent. of glycogen. The liver of one fed upon starch and grape sugar afforded 15·4 per cent. of the same product; that of another whose food had been starch and cane sugar, gave 16·9 per cent. Further experiments upon animals of the same species showed that the large formation of glycogen under a diet of starch and sugar was not lessened by the admixture of their food with phosphoric acid, liquor potassæ, acetate or citrate of potash. Upon a diet of gum-arabic the glycogen was lessened. With olive oil, gelatin or albumen, this hepatic product was absent or existed only as a trace.

These important observations may be supplemented by those of Dr. M'Donnell,[2] from whom I quote the following table.

[1] Pavy 'On Diabetes,' ed. 2nd, p. 90.

[2] M'Donnell 'On the Functions of the Liver,' p. 14.

Average quantity of amyloid substance (or glycogen) found in the entire liver of animals fed for some days on the following materials.

	Sugar and Starch	Fat	Gluten Bread	Gelatin
Dogs . .	980 grs.	hardly a trace	125 grs.	none
Rats . . .	7 „	ditto	3 „	none
Pigeons . .	25½ „	—	1 „	—
Rabbits . .	45 „	—	8½ „	—

Thus much glycogen appears under sugar and starch, less with gluten bread, while with fat and gelatin there is little or none. These observations as bearing upon fat and gelatin have much practical importance. With gelatin in particular, they give more general truth to the observations of Pavy, since they extend to dogs and rats conclusions which the former observer based upon the examination only of rabbits.

Thus experiments on animals, the results of which, since they hold good with different species, warrant us in believing that the same rules extend also to man, show that the hepatic glycogen attains its greatest amount with starch and sugar, little difference being observed between these two hydrocarbons; that it is formed, though more scantily, from albumen, fibrin and gluten; while animal oil or fat, vegetable oil, and gelatin, fail entirely, or almost entirely, to supply the means for its production. The importance of these deductions can scarcely be overrated in their practical bearing upon the treatment of diabetes.

Disposal of glycogen.

Admitting, as probably most of my readers will be willing to do, that sugar derived from the transformation of glycogen is discharged during life into the blood, it may be asked what becomes of it? Bernard[1] formerly thought that it was consumed in the lungs, but he now, with other physiologists, believes it to be used in the nutrition of the tissues, more particularly of the muscles. By exciting the sciatic nerve, and so increasing the muscular activity of the leg, he showed that the sugar in the blood of the limb underwent energetic destruction.

Dr. Harley[2] found that the blood in the left side of the heart of a cat contained exactly the same quantity of sugar as that in the right, so that no loss had occurred in transit through the lungs. That the blood lost sugar in the tissues appeared by the

[1] Bernard's 'Lectures on Diabetes,' 'Medical Record,' Oct. 8, 1873.

[2] 'The Urine and its Derangements,' p. 234.

diminution of this substance in venous as compared with arterial blood. These observations justify us in believing, what common experience teaches, that sugar plays an important part in the nutrition of the body.

Glycogenic Ferment.

It is necessary to say a word as to the supposed fermentive action by which the glycogen is converted into sugar. Glycogen out of the body remains unchanged so long as it is unmixed; the presence of blood, saliva, pancreatic juice, and of many other organic fluids causes its rapid conversion. Thus in the liver, whether alive or dead, the glycogen is continually undergoing transformation. Extracted and isolated, it retains its character, but immediately undertakes the saccharine change on the addition of saliva or blood.

The existence of a special ferment has been inferred, though it has not been isolated. Whether there be one widely distributed agent of this nature, or whether, as is equally probable, there be several which thus destroy the stability of the animal starch, it is clear that as with vegetable starch the conversion into sugar needs co-operation from without. There is something which plays the part of diastase.

Bernard[1] supposes that while glycogen resides in some hepatic cells, the ferment has its seat in others; the contact or separation of the two substances being ruled by the nervous system.

Schiff attributes to this invisible ferment a leading part in the production of glycosuria. In his view this symptom is the result of the excessive formation not of glycogen but of the ferment, the superabundance of which causes excessive saccharine conversion, though the sugar-forming material has undergone no increase. This improbable theory appears to have been sufficiently confuted by Dr. Pavy, who injected saliva, which has typically the diastatic property, into the blood without giving rise to any saccharine change in the urine. Probably the human body has always a superabundant supply of some or other of the various materials which have the property in question; so that whatever may be the immediate cause of glycosuria we cannot attribute it to any excess of the hypothetical ferment.

[1] 'Lectures on Diabetes,' 'Medical Record,' 1873, p. 676

On the part of the Nervous System in the Production of Glycosuria.

So far it has been shown that sugar is made in the healthy body, but in scarcely greater quantity than can be consumed by the needs of the system, since the urine, though believed commonly to contain a trace of this substance, gives exit to so small an amount that it cannot be recognised by the ordinary methods. The question next arises why and how the process becomes so exaggerated or perverted that enough sugar escapes with the urine to give rise to the phenomena of diabetes. In answer we are again indebted to the genius of Bernard. To test the influence of the pneumogastric nerves upon the glycogenic function of the liver he punctured the floor of the fourth ventricle immediately above their source, and the urine at once became saccharine. But further experiments showed that the effect was not produced as at first imagined by a direct irritation of the vagi. Puncture of the medulla made the urine saccharine notwithstanding that these nerves were cut. If without puncture of the medulla the trunk of the vagus were divided and the cut ends galvanised, it was found that no glycosuria followed such irritation of the part of the nerve in connection with the liver, while this symptom at once resulted from the application of the poles to the cerebral segment of the nerve. Hence the pneumogastric takes no share in conveying the glycosuric irritation from the brain to the viscera, though capable of conducting it in the contrary direction. Bernard inferred that the route lay along the spinal cord and splanchnic nerves to the vaso-motor nerves of the liver, the influence being of a kind to cause relaxation of the blood-vessels with consequent increase of circulation and exaggeration of function.

Sugar puncture.

The subject has been elaborated by successive experimenters, among whom may be mentioned Pavy, Schiff, Eckhard, Cyon and Aladoff, who have defined the route of what for the sake of convenience we may term the *glycosuric influence*, from the brain to the liver, and have afforded data which will enable us to draw general inferences as to its nature.

To epitomise the results :—

Schiff [1] found feeble glycosuria to ensue from vertical sections

[1] 'Journal de l'Anatomie et de la Physiologie,' 1866, p. 376.

of the optic thalami or cerebral peduncles; Pavy,[1] on the other hand, severed the cerebrum from the rest of the encephalon by section through the peduncles without any such result; an observation perfectly reconcileable with the preceding, since the effect is due, as will presently appear, not to the loss of nerve substance but to the irritation engendered in the cutting.

Glycosuric irritability widely distributed.

More marked diabetes, according, to Schiff, followed lesions of the Pons Varolii or of the middle cerebellar peduncles. Section of the posterior peduncles of the cerebellum also gave rise to glycosuria, but this symptom in its greatest intensity followed puncture of the medulla as practised by Bernard. The region most sensitive in this respect is limited in front by a line connecting the origins of the auditory nerves, and behind by one joining the origins of the pneumogastrics, though a feebler association with saccharine urine extends beyond these bounds. It is said that wounds of the medulla to produce glycosuria must necessarily involve the olivary fasciculi; it is at least certain that injuries affecting these columns produce the symptoms with great readiness; a fact which has additional interest in connection with the lesion of the olivary bodies, which, as I shall presently show, is almost invariably present in human beings who have died of diabetes.

Decapitation, or transverse section of the medulla, causes glycosuria. Section of the cord may cause this symptom though it does not necessarily do so. Pavy cut the cord between the second and third vertebræ, life being retained for a time by means of artificial respiration, without giving rise to the symptoms in question. On the other hand, prolonged diabetes followed breaking up of the cord as practised by Schiff opposite the second dorsal vertebra, and the urine was also made saccharine by various injuries about the roots of the brachial plexus; while some experiments testified that this result followed section of the posterior, others that it followed section of the anterior and lateral columns.

Thus the part of the cerebro-spinal axis, experimental injuries of which have been found to render the urine saccharine, reaches from the optic thalami to the lower end of the cervical enlargement; while within these bounds the faculty is extensively though not equally distributed.

Thence tracing the glycosuric influence to the viscera, the

[1] See Pavy 'On Diabetes,' ed. 2nd; also papers by the same author; 'Proceedings Royal Society,' vol. x. p. 27; and 'Guy's Hospital Reports for 1859.'

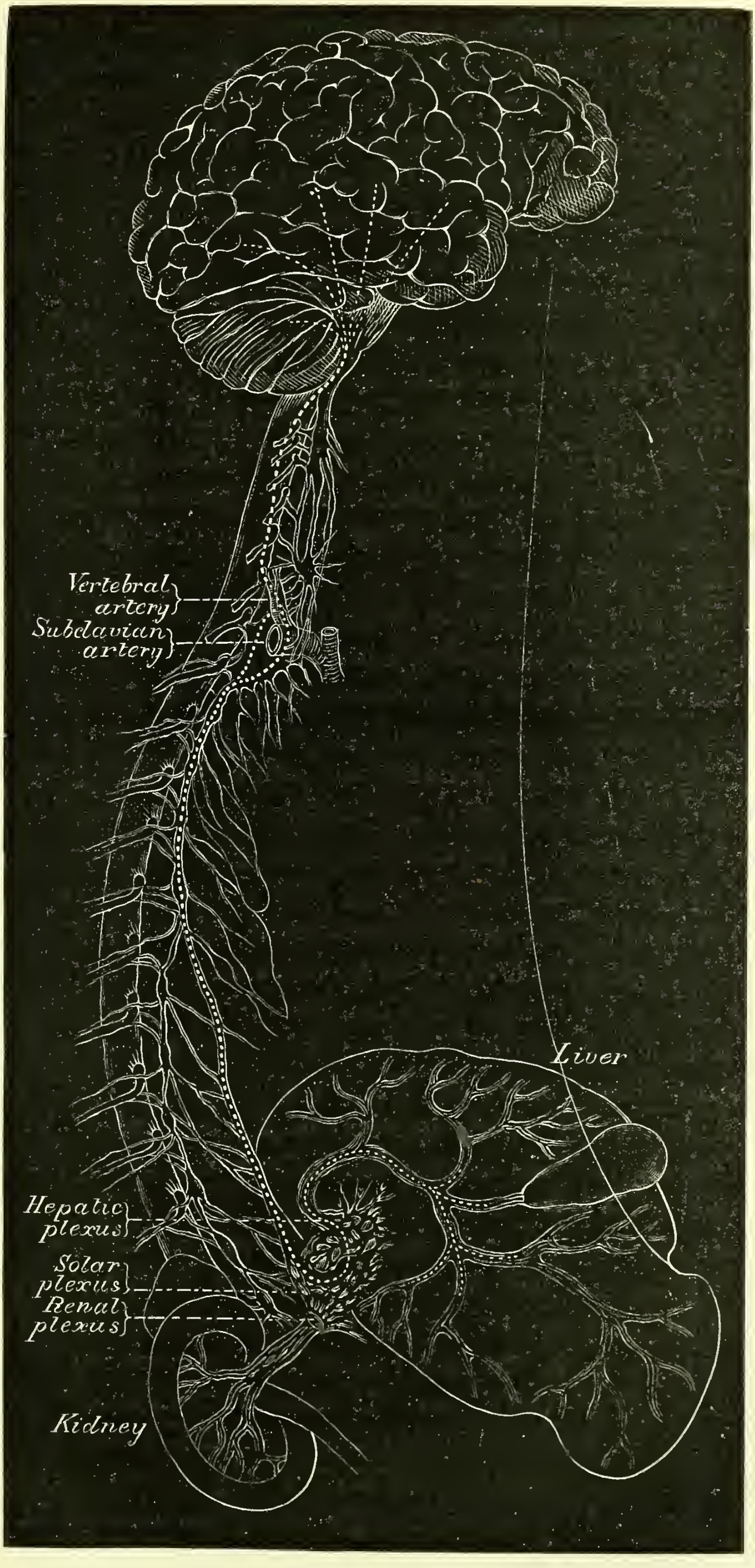


FIG. 1.—The dotted line shows the course of the glycosuric influence from the brain to the liver by the spinal cord, last cervical ganglion prevertebral ord and great splanchnic nerve.

results of experiments appear to indicate that it leaves the cord in the cervical region by filaments in connection with the sympathetic, to descend upon the vertebral artery to the third cervical ganglion, whence by branches which accompany the subclavian artery, it reaches the first dorsal ganglion, and thence is conveyed by the prevertebral cord, the splanchnic nerves, and the solar plexus to the liver.

The preceding figure shows diagrammatically the origin of the glycosuric irritation and its course from the brain to the liver, according to the experimental researches which have been referred to. For the sake of distinctness the brain and cord are shown in surface, but it is not meant to be implied that the irritation is superficial. Since this was planned I have seen a similar diagram by Dr. Brunton in an excellent paper on the subject in the 'British Medical Journal.'[1]

Travels by the spinal cord and sympathetic.

As to the observations by which this route has been mapped, the pneumogastric nerves have been excluded by experiments to which reference has already been made. With regard to the sympathetic in the neck, it has been shown that section of the connecting cord never renders the urine saccharine, while destruction of the upper cervical ganglion does so sometimes, but not with constancy. At the same time glycosuria ensues from cerebral puncture notwithstanding that this portion of the sympathetic has been severed. We cannot therefore fail to infer that the cervical gangliated cord has no necessary part in the causation of saccharine urine. The condition, however, appears invariably to result from division of the filaments upon the vertebral artery, destruction of the third cervical ganglion, or severance of the branches which under the name of the annulus of Vieussens pass thence with the subclavian artery to the upper dorsal ganglion.

Below this point the results of section are less simple. Glycosuria has not been found to follow the cutting of the dorsal prevertebral cord, or of the splanchnic nerves, or of all the nerves entering the liver in the lesser omentum, comprising the entire nervous supply of the organ. It has next been ascertained that after section of the splanchnic nerves or the branches leading thence to the liver, puncture of the medulla no longer causes the urinary change in question, though when this change has been

[1] January 1874.

previously produced by cerebral puncture, it does not cease upon section of the splanchnics.

To these observations it may be added that Schiff has found the urine of rabbits to be slightly saccharine after section of the nerves either of the upper or the lower extremities. It may be observed that glycosuria produced by any of the injuries described which allow of the survival of the animal, is transient, usually passing off in from five to twenty-four hours, when the irritation of the hurt may be supposed to have abated, but before it is conceivable that the severed fibres have been restored to continuity and use. The symptom was most enduring in the division of the cord as practised by Schiff in rats. After this necessarily fatal operation the urine was found to be saccharine until death, which in some instances did not occur until the twentieth day.

Irritative rather than paralytic.

These observations concur to show that the influence which gives rise to artificial traumatic diabetes is irritative rather than paralytic. On the supposition that the glycosuria springs simply from the interruption of the vaso-motor nerves and consequent paralytic dilatation of the vessels of the liver, no satisfactory explanation presents itself of the absence of this result after division of the splanchnics which are in the direct line of hepatic innervation, or of its presence after injuries of the sciatic nerve or upper cervical ganglion which are out of it. Severance of the entire nervous connections of the liver not only does not cause glycosuria but prevents it. Thus we must conclude that this condition arises not from mere deprivation of nerve influence, but from an unnatural nervous irritation which the splanchnics convey to the liver. Regarding the glycosuric nervous influence as something more than mere loss or interruption of function, as consisting not of the absence of healthy but the presence of morbid excitement, we see points of analogy between this and other disorders connected with perverted nervous action. In tetanus the peripheral irritation conveyed by a nerve to the cord causes in that structure dilatation of vessels and hyperæmia of tissue with consequent exaltation of the function of the organ to which the vessels belong. Artificial diabetes, caused like tetanus by nervous lesion, differs from it rather in the seat of the resulting organic disturbance than in the nature of the process by which it is produced. The morbid impression, which may within certain limits vary much both in position and in kind, has its origin in some part of the nervous system remotely connected with the vaso-motor system of the liver. Its effect appears in

the dilatation of the hepatic vessels, with consequent exaggeration or disturbance of function.

The splanchnic nerves are the conductors of the irritation, playing the part of the afferent nerve in tetanus, the timely cutting of which will prevent the development of the disease.

The production of hyperæmia, or even inflammation as the result of a remote or reflected nervous irritation, is a familiar fact in pathology, and may be hypothetically explained by the contraction of the longitudinal fibres of the blood vessels and consequent increase of their calibre.

Sugar made instead of glycogen.

So far all is clear; but at this point a doubt presents itself. The ultimate issue of the vascular excitement is an over-production of sugar: but it is uncertain whether this is preceded by, and consequent upon, an over-production of glycogen, in which case the function of the liver would be increased but not altered in character; or whether the action of the liver is so far interfered with by the hurry of circulation as to form sugar directly, out of the materials which should have formed glycogen, but without passing through this intermediate stage. The latter supposition is supported by certain facts of disease, as well as by some experiments, which may be referred to by anticipation, relating to artificial glycosuria. When this state has been induced in the rabbit by woorara, sugar injected into the stomach appears in the urine but causes no deposit of glycogen in the liver. In a state of nature with this animal the converse holds; injected sugar makes glycogen in the liver but does not appear in the urine.[1]

GLYCOSURIA FROM HEPATIC IRRITATION.

Irritation of the liver by the insertion of needles, or the passage of galvanic currents through its tissue introduced by their means, have been found to cause glycosuria—acting probably by causing hyperæmia of the organ. A similar result has been stated to follow the tying of the renal vessels in frogs[2] so as to direct more blood to the liver; and in the hands of Dr. Harley saccharine change has been caused by the injection of alcohol, ether, or ammonia into the portal vein. In all these circumstances it would seem that the discharge of sugar is connected with the exaggerated hepatic circulation which the irritant, be it what it may, has produced.

[1] W. F. Dock, 'Pflüger's Archiv.' (v. p. 571–583). 'Brit. Med. Journal,' 1872, p. 276.

[2] Schiff.

Respiratory and Toxic Glycosuria.

With the belief that the sugar derived from the liver was normally consumed in the lungs, and that diabetes would result from a suspension of the supposed pulmonary oxidation and consequent retention of the sugar in the blood, much attention has been devoted, especially by Reynoso,[1] to disturbances of respiration in connection with Glycosuria.

It has been shown that this result may be produced in healthy animals either by mechanical impediments to the breathing, or by the inhalation of vapours or gases[2] unfit for the needs of respiration, or by the administration in other ways of poisons some of which at least arrest or notably disturb this vital function. These observations admit of no question, although the view which suggested them is not that in which they must be now regarded, since the bulk of the sugar which the blood receives appears to be used in the tissues rather than in the lungs. It is not impossible that in such circumstances the glycosuria is caused by the perturbation of the glycogenic function, owing to the retention of venous blood in the liver from pulmonary obstruction.

Dyspnœa.

Passing to detail:—first as to mechanical impediments; Reynoso found the urine to be saccharine, though not constantly so, in strangled and drowned rabbits; and Bernard produced a strongly saccharine state of the same secretion in dogs by keeping them in a state of incomplete strangulation for half an hour. It is stated that sugar is often found in the urine of human beings suffering from diseases of the respiratory organs, more especially in whooping cough: it would seem, however, that though traces of sugar are sometimes found after fits of whooping cough, yet that in the human subject the connection between dyspnœa and glycosuria rarely appears. Dr. Roberts suggests, in accordance with what we know of the disappearance of glycogen under disease, that the pyrexia or other disturbance of health commonly associated with dyspnœa of morbid origin has led to the removal of this material.

I have examined many cases of croup in which the breathing

[1] Mémoire sur la Présence du Sucre dans l'Urine, et sur la Liaison de ce Phénomène avec la Respiration.' 'Annales des Sciences Naturelles,' 1855, p. 120.

[2] Loc. cit. p. 131.

has reached the extreme of difficulty, and others of bronchitis in which dyspnœa to blueness has existed, without finding a trace of sugar in the urine. The following instance is an exception.

Croup.

A girl seven years of age, whom I treated at the Hospital for Sick Children, had croup with apparently hopeless severity. Under antimony, at the rate of half a grain an hour, the dose diminishing with the symptoms, she recovered. Five days after her admission, on the approach of convalescence and the discontinuance of the remedy, the urine was found to be passed with frequency and to be considerably saccharine. It averaged about a pint in the twenty-four hours, and had a sp. gr. often as high as 1030. The sugar persisted; a trace was found when the child was last seen six weeks after it was discovered. Though the urine was not examined previously, the extreme rarity of diabetes at the age of seven warrants us in assuming that the secretion was free from sugar previous to the croup. It may be added that no symptoms of diabetes attended the glycosuria in this instance. It was probably produced either by the croup or the antimony. In the absence of any reason to assign the change to the metal, it must be attributed to some change consequent upon the dyspnœa; possibly to hepatic congestion or minute cerebral extravasation.

Irrespirable vapours.

Pursuing the investigation by the pulmonary clue, Reynoso found sugar in the urine after the inhalation of many vapours and gases unsuited for the purposes of respiration. Among these he instanced ether, chloroform, Dutch liquid; nitric and acetic ether; hydriodic, hydrobromic, and chloramylic ethers; aldehyd; benzol and acetone. He found the same state of the urinary secretion after slow suffocation by sulphuretted hydrogen, carbonic acid, and hydrocyanic acid; and later observers have found it to follow the breathing of carbonic oxide and nitrite of amyl. Nitrite of amyl perhaps may with more likelihood be supposed to act directly on the vaso-motor nerves of the liver as well as elsewhere; but with regard to others, looking at the varied inhalations to which glycosuria has been traced, we can hardly avoid the conclusion to which Reynoso was led, that the embarrassment of the respiratory function, caused more or less by all, is the means by which the common result has been produced. According to this observer, all gases or irrespirable vapours which determine anæsthesia cause glycosuria.

With regard to chloroform, some discrepancy of opinion has

arisen from the fact that this agent has itself a slight effect in causing the reduction of copper generally relied upon as distinctive of sugar. Dr. Pavy, who has examined the urine in many cases after the surgical use of chloroform, is of opinion that the reaction is such as to indicate the presence of a small though real amount of sugar. Dr. Bence Jones found slight but distinct evidences of sugar in the urine of a person who had been for twenty-four hours under the influence of chloroform. Dr. Beale[1] failed to satisfy himself of the presence of this substance in six persons who had been placed under the influence of the same anæsthetic.

It is interesting to place in apposition with the supposed glycosuric effect of chloroform the observations of Bernard, that its inhalation in the cutting of the sympathetic prevented the saccharine change which would otherwise have taken place in the urine. It probably thus acts by diminishing the irritability of the injured nerve.

Other toxic and medicinal substances, administered in different ways, also cause glycosuria. Some have been thought to cause this result by means of respiratory embarrassment; with regard to others, no such theory can find place.

Bernard showed that[2] the injection of woorara caused, firstly, increased saccharinity of blood, and secondly, the discharge of sugar with the urine; and that these results occurred not only when the dose had been such as to paralyse the muscles of breathing and necessitate artificial respiration, but also when the quantity given was not enough to arrest the natural performance of this function. He considers that the poison causes glycosuria by paralysing the vaso-motor nerves of the liver, thus making its vessels larger and its circulation more active, in much the same way as the circulation in this organ is enhanced by puncture of the floor of the fourth ventricle. Woorara causes salivation, probably by exaggerating in a similar manner the circulation of the glands concerned. Woorara.

I have already referred (page 18) to the statement that woorara causes glycosuria without any intermediate formation of hepatic glycogen; which if true shows that it is at least possible that diabetes may be due to the elements of sugar being hurried through the liver and poured in a saccharine form into

[1] 'Kidney Diseases, etc.,' 3rd ed., p. 269.

[2] 'Lectures on Diabetes,' 'Medical Record,' 1873, p. 694.

the blood, having escaped the transformation which might have turned them to other uses.

Other drugs.

Glycosuria has also been observed after poisoning by morphia and strychnia. Morphia according to Bernard brings about this result in a similar manner to woorara. Schiff, on the other hand, perhaps less consistently with our present knowledge, attributes the glycosuria of woorara and strychnia to embarrassment of respiration, and maintains that if after poisoning by strychnia artificial respiration be performed in a manner closely resembling that of nature, this change in the urinary secretion does not occur. Glycosuria has also been found to follow the administration of nitrate[1] of uranium, salts of mercury, phosphoric acid, and some other drugs. Some of these, and among them phosphoric acid, may be supposed to act as direct irritants of the liver.

The glycosuric effect of phosphoric acid was pointed out by Pavy; it resulted whether the solution was introduced into the blood directly or by the alimentary canal.[2]

Physiological Summary.

Before proceeding to the organic lesions associated with diabetes in the human subject, it may be worth while, in a few sentences, to reckon up the bearings of physiology upon the subject.

Sugar a normal product.

Sugar is normally made in the liver, present in the blood, and used in the tissues; but whether this is the main or only a subordinate issue of the hepatic glycogen is at present undetermined.

The sugar in the urine comes from the blood. When the blood contains more of it than is used in the system the superfluity escapes chiefly by this secretion.

The capacity of the blood for sugar is limited. In the dog,[3] as Bernard has shown, glycosuria ensues when the sugar in the blood reaches 0·25 per cent. With man the saccharine capacity of the blood and the point of over-

[1] Léconte. [2] 'Guy's Hospital Reports for 1861.'
[3] 'Lectures on Diabetes,' 'Medical Record,' 1873, p. 707.

Glycosuria its lessened consumption or increased supply.

flow are less known but perhaps not less definite. The question of sugar in the urine therefore reverts to superabundance of sugar in the blood. Theoretically this may be due either to diminished consumption or increased supply. The tissues or lungs, on the first supposition, may no longer claim their dole of sugar, but leave it to accumulate and escape. This view however is inconsistent with the facts of disease.

To take the lungs first in deference to the older views—if they provide sugar with an exit we fail to trace diabetes to its closure. Although pulmonary disorganisations may complicate the later stages of the disease, it is certain that this follows instead of preceding the diabetic state. Nor can we commonly find any other justification, whether in the mechanism of the respiratory organs or the surroundings of the patient, for assuming that deficiency of pulmonary oxidation has anything to do with its causation. At the outset of diabetes the lungs are commonly healthy and aëration, as far as we can judge, normal. Although it must be allowed that certain respiratory embarrassments may be followed by slight and temporary glycosuria, yet it may be suggested that this result is immediately due rather to hepatic congestion than insufficient pulmonary combustion. It is certain that diabetes as it occurs in the human subject is not to be traced to cyanosis or dyspnœa, and we may fairly conclude that whatever consumption of sugar is proper to the lungs (a matter not without doubt), we cannot attribute diabetes to its deficiency. And as to the tissues, we are equally without evidence that any failure in their power of saccharine assimilation precedes the disease. A person becomes thin because he is diabetic, not diabetic because he is thin.

No evidence of its lessened consumption.

Sugar has been supposed to become converted in the tissues, more particularly in the muscles, into lactic acid by the aid of a ferment, and it is theoretically possible that the want of this ferment may allow the sugar to remain unchanged, accumulate and escape; but this hypothesis is not consistent with the fact that animals

may, as I have found, be frozen to death, a process which must be supposed to arrest all fermentive action, without being rendered glycosuric, nor is it consistent with the clinical history of diabetes, which gives us no reason to connect it with any antecedent failure in the general nutrition of the body.

To be referred to increased supply

We are fain to conclude that the superabundance of circulating sugar, essential to diabetes, is a matter of increased supply, not diminished consumption; and thus the problem limits itself to the intrusion in excess of sugar into the blood.

The amount of sugar which finds entrance into the blood must, in the ordinary circumstances of the human subject, depend either upon the amount put into the stomach; upon the amount transmitted as such from the stomach to the general circulation; or upon the amount developed within the body.

by excess of saccharine food,

Taking these conditions in order, first as to the excessive introduction of sugar; man or beast may normally discharge by the kidneys sugar which has been put in excess into the stomach. Cane-sugar ingested in no larger amount than the organs can deal with, is stored as glycogen in the liver, to be yielded up as grape-sugar. Bernard ingeniously[1] showed that when cane-sugar was given to a dog in excess—a large quantity of syrup being injected into the stomach—some reached the urine without intermediate transformation into glycogen, since it contained lævulose, a product of cane, not of grape-sugar. Thus, of much sugar, some may elude organic transformation and pass almost directly from the stomach to the kidneys. This is *normal alimentary glycosuria.* It is transient as its cause. This in the human subject is rather a theoretical possibility than an occurrence of practical frequency.

Passing now to glycosuria from the increased transmission, or in other words from the diminished assimilation, of sugar, we enter the confines of disease.

[1] 'Revue Scientifique,' 2nd series, vol. iv. p. 1066.

This may be termed *abnormal alimentary glycosuria.*

Ingested sugar and starch are normally intercepted by the liver, stored as glycogen and applied to use and nutrition, in modes which we do not fully understand, but probably not wholly and immediately as sugar. Under the hyperæmia of nervous irritation, the liver, with its widened vessels and hurry of circulation, seems to lose its assimilative grasp of sugar and starch, so that these hydro-carbons, eluding the glycogenic transformation necessary for their useful application, enter the general circulation as sugar, only to be cast out. Clinical observation supports the view that there is a form of diabetes which thus depends, not on the making of sugar within the organism, but on its passage as such from the stomach to the blood. The glycosuria in these cases depends on the ingestion of sugar and starch, and ceases when these aliments are wholly withdrawn. Clinically this often seems to be a first or incomplete stage of diabetes, a stage sometimes quickly replaced by graver failure, sometimes intermittent, indefinitely prolonged, and comparatively harmless.

by failure in the assimilation of such food,

Proceeding now from the increased transmission of sugar to its increased development, we reach diabetes in the severe and common shape, in which sugar is excreted, though neither saccharine nor amylaceous matter have been taken in.

or by abnormal making of sugar.

The excess of sugar may be derived from glycogen, resulting either from its increased production or its increased saccharine transmutation; or it may, as experiments with woorara suggest, be made instead of glycogen out of its materials.

This brings us within the region of debate.

Considering first the possible origin of the saccharine excess in glycogen, we must attribute it either to the amount of glycogen formed, or to the proportion of it which is thus converted. Following this road we here come to a divergence.

If, as held by Pavy and M'Donnell, glycogen is not

normally converted into sugar, diabetes may consist in its perversion to that end. If, on what seems preponderating evidence, we accept the view that sugar is in the living body a proper and necessary issue of glycogen, we may see in diabetes only an excessive formation of this liver-starch.

First, as to diabetes by transmutation of glycogen. Pavy believes that hepatic sugar is normally only a post-mortem product; and diabetes, so to speak, a foretaste of mortality. The disease in this view consists in the withdrawal during life of the nervous influence necessary to withhold the glycogen from turning into sugar. Thus a cadaveric change occurs before death, and the diabetic person, as Bernard has put it, carries the liver of a corpse. But if we are satisfied, as I think we may be, with the evidence that sugar is a product of the living and healthy liver as well as of the dead, this point of view cannot be maintained.

Excess of sugar probably not from increased change of glycogen,

Passing from cadaveric transmutation of this animal starch to transmutation by morbid ferments—a theory which has also found place—this hypothesis as to the source of the sugar may be dismissed, firstly, as inconsistent with the probable constant superabundance in the body of substances capable of acting catalytically upon the unstable amylaceous product, and secondly, as directly contradicted by experiment.

Not accepting, therefore, either view of the saccharine perversion of liver-starch as satisfactorily explaining the excessive making of sugar which constitutes the diabetic state, we are thrown back upon two alternatives; the one being the superabundant formation of glycogen and consequent superabundance of its saccharine derivative; the other, the making of sugar instead of glycogen.

That diabetes is mere hyperglycogenesis—superabundance of healthy glycogen—is not absolutely disproved. Bernard, the supreme genius of modern physiology, describes diabetes as 'an[1] exaggeration of nutritive

[1] 'Lectures on Diabetes,' 'Medical Record,' 1873, p. 741.

phenomena.' But there are considerations which militate against this view.

A gland whereof the circulation is hurried, perturbed, and distinctly abnormal as is that of the liver in diabetes, can hardly be supposed to suffer no further change in action than magnification of its healthy product. In whatever organ we trace its results, we find that congestion does not merely exaggerate but always alters function. The congested kidney does not secrete natural urine, congested membrane does not pour out mucus or serum which is exactly that of health. And it has been shown, at least with regard to wooraric diabetes, that glycosuria may exist without the formation of glycogen.

nor from its increased production,

Perhaps the view most consistent with our present knowledge is that with the diabetes in which sugar is made in the body (out of the protein substances) the essential vice is a perversion of hepatic action, which while it does not hinder and possibly exaggerates the disruption of the protein bodies, substitutes in the issue sugar for glycogen. Thus a material which should be retained as glycogen to form sugar, probably only in small proportion while it ministers in other ways to nutrition, is replaced by sugar of which the bulk is necessarily expelled. This view is consistent with many observations upon animals, though difficult of confirmation in the human subject, owing to the time which must necessarily elapse between death and the examination of the liver, and the fleeting nature of the distinction between glycogen and sugar.

but by the substitution of sugar for glycogen.

If this view be correct, both forms of diabetes—the slight or early kind in which sugar is only transmitted, ceasing from the urine when sugar and starch are withdrawn from the food, and the more severe kind in which the sugar discharged is made in the body out of albumen and the like—may equally be described as failure of the liver to make glycogen, or the due proportion of glycogen, out of what should form it. In the first instance the liver loses its hold only of some of the superabounding

glycogenic material of sugar and starch, but can deal normally with the smaller proportion presented in nitrogenous food. In the second case the glycogenic elements from both sources elude transformation. The two kinds would thus appear to be merely different degrees of imperfection in hepatic glycogenesis; and that they are closely allied is evident from the manner in which they pass into each other.

The imperfect (or in the other view the excessive) formation of glycogen has its immediate cause in an unnatural excitement of the circulation within the liver, which may be due to direct irritation of the organ, to mechanical expedients which increase the quantity of blood sent to it, and apparently to conditions like respiratory embarrassment which prevent the free discharge of blood from it.

But of all the causes which, presumably acting through the blood vessels, excite the gland to the action necessary to diabetes, nervous disturbance is the chief. This in its nature appears to be irritation rather than interruption, analogous to that which causes tetanus, the incidence of irritation in the one case being upon the cord, in the other upon the liver.

From hepatic disturbance, usually of nervous origin.

In position the nervous irritation of glycosuria has a wide range. It may arise in many parts of the sympathetic; in the cervical region of the cord; or anywhere in that great cerebral tract which lies between the cord and the crura cerebri. The medulla oblongata contains the structures the irritation of which causes the exaggeration of function with the greatest facility and profusion. Impressions pass thence to the liver, first through the cord, afterwards by a route which has been sufficiently defined. This chain of communication represents the cerebro-spinal, or excitor nerve of the gland. Every gland, as Bernard first showed with regard to the salivary, has nerves of two kinds which are derived from different sources and have antagonistic functions, one stimulating, the other repressing secretion. The vaso-motor nerves

which belong to the sympathetic contract arteries, lessen blood supply, and diminish secretion. The cerebro-spinal nerves accelerate circulation, dilate ducts, and excite to secretion and function. The cerebro-spinal nerve of the liver has its origin at the fourth ventricle. Irritation at or directed upon this spot, or striking the nervous chain between it and the liver, causes, if transient, temporary glycosuria, if permanent, diabetes.

CHAPTER II.

PATHOLOGY.

PERHAPS the general estimation of the morbid anatomy of diabetes might be aptly expressed by a blank. It has been, and apparently is commonly, thought that no substantial changes are necessarily antecedent to the disease, though various wasting processes may be caused by it. This 'purely chemical derangement' has been regarded as independent of structural alteration; as if the organs in the misapplication of nutriment were guided by mere perversity. But beyond the inherent improbability that this persistent and fatal malady should be other than the expression of irremediable changes in the structure of vital organs, the discoveries of Bernard and his followers, showing the dependence of glycosuria upon artificial injuries, are enough to suggest careful enquiry into the state of the nervous system in persons in whom the same symptom has been naturally induced.

Upon this hint, attention has of late years been directed to the brain in diabetic subjects, with the result in exceptional cases of finding softening, intra-cranial growths, or some other self-evident lesion as a complication of the disease. M. Luys found in two instances softening and discolouration of the medulla with degeneration of the nerve cells; these changes, however, he regarded as consecutive upon the malady, not antecedent to it. Other examples have been reported in which softening, injection, or discolouration existed about the fourth ventricle.[1]

[1] I have referred to some cases of this kind in the 'Medico-Chirurgical Transactions for 1870.' M. Luys' cases, two in number, are reported in the

More rarely intra-cranial tumours or morbid growths have been found. But such obvious signs of disease were rare and evidently exceptional as accompaniments of diabetes; none occurred with such regularity as to suggest any necessary connection between the urinary disturbance and such cerebral changes, and their occasional detection threw little light upon the pathology of the overwhelming majority of cases in which the brain to ordinary examination was natural. Morbid anatomy so far having furnished nothing which could displace the functional or purely chemical view of the disease, I determined to examine anew with the improved means of modern microscopic research, and as comprehensively as I could, the organs of diabetic subjects. The results, which have been corroborated by subsequent observations, are given in detail in the Medico-Chirurgical Transactions for 1870. They point to the inference that diabetes is produced by substantial and constant changes in the nervous centres, none the less significant because, as with many other diseases of these structures, they are such as ordinarily to elude the naked eye. They are such indeed as to link symptoms with lesions as closely with natural as with artificial glycosuria, and to give to diabetes a definite place among diseases of the nervous system.

Diabetes, an isolated and well-defined disease in which the production of sugar is the leading symptom and chief source of danger, must not be confused with the glycosuria which is an unimportant, generally an unnoticed, and almost to be called an accidental complica-

'Bulletins de la Société Anatomique,' 1860, p. 247, and in the 'Comptes Rendus de la Société de Biologie,' p. 24.

M. Lanceraux ('Bulletins de la Société Anatomique,' 1860, p. 221) describes the post-mortem examination of a diabetic subject in which the brain was softened, the ventricles dilated and their walls discoloured, while there was much injection with small extravasations about the calamus scriptorius, the nerve cells in this neighbourhood being broken down and occupied by yellow granulations. M. Martineau, 'Bulletins de la Société Anatomique,' 1861, p. 290, describes changes about the fourth ventricle in a case of diabetes similar to those described by M. Luys. See also a case in which a somewhat similar condition was observed by Monveret ('Gaz. des Hôp.' Jan. 11, 1862).

tion of various cerebral lesions, extravasations, tumours, and contusions.

Brain to naked eye.

The brain of diabetes is almost invariably free from tangible or obvious disease, and to rough examination natural. It is generally firm in texture; not more so than the healthy brain sometimes is, though if its consistence excites observation it is almost always in this direction. In vascularity and colour it usually passes without notice. Sometimes it is obviously congested in whole or part, rather from the exaggeration of vessels within reach of the naked eye than from any minute or capillary injection of tissue. A practised and careful eye will often detect a fine porosity or cribriform appearance in limited patches of the white matter as if closely beset with pin-holes, each puncture containing a vessel much smaller than itself. More rarely considerable cavities, such as might hold peas, are seen, especially in the pons in connection with one of the processes of the pia mater. These, large and small, become more evident, and are seen to be somewhat generally scattered, after the hardening of the brain in spirit or chromic acid so as to allow of the cutting of clean sections. Under the microscope these excavations become conspicuous objects. The fluid around and within the brain of diabetic subjects is generally slightly in excess though seldom markedly so; the brain is sometimes in the condition described as wet, though in the majority of instances the condition in this respect does not differ from what is commonly noticed after death from causes unconnected with cerebral disturbance. I have never known it to be enough to flatten the convolutions. Usually the fluid in the ventricles and under the arachnoid is colourless and limpid, though one instance came under my knowledge in which the fluid in the latter situation was blood-tinged. In this case the brain was generally and unusually injected.

The spinal cord, like the brain, seldom presents morbid changes obvious to the naked eye, though it sometimes appears to be irregularly injected, and now and then it

may be noticed in the fresh section, and more strikingly after hardening, that the central canal is dilated or the commissure broken.

MINUTE CHANGES IN THE NERVOUS CENTRES.

Minute examination of the brain and cord in diabetes, started with the naked eye and pursued with the microscope, shows changes of such constancy that we must needs suppose them to be essential to the disease.

Since I first noticed these changes in the year 1868[1] I have especially examined the nervous centres in eleven cases of diabetes and have found them in all.

The microscope is not necessary for their detection, though it is for their description. For their recognition it is only necessary that the brain should be carefully looked at while fresh, or for their more clear display should be hardened in any way which allows of the exposure of clear and sharp sections. Large excavations, and pores in cribriform arrangement, thus become evident to the naked eye which the microscope will explain in detail.

Excavations.

The excavations are found about arteries or in positions which arteries have once occupied. They are sometimes globular and at their maximum such as would lodge peas. Often, they are elongated and narrow, and may be described as tunnels directed by the course of vessels. They are caused by a destruction and absorption of the nervous matter along the course of arteries, and are, at least in some instances, caused by an escape of the contents of the vessel into the surrounding tissues, with consequent degeneration, softening, and removal of the nervous matter which has been permeated by the intrusion. The escape appears to be rather of corpuscles by

About arteries.

[1] For a minute account of these observations I may refer to a paper which was communicated to the Medical and Chirurgical Society in January 1870, and is published in the 'Transactions' for the same year.

Beginning in hæmorrhage.

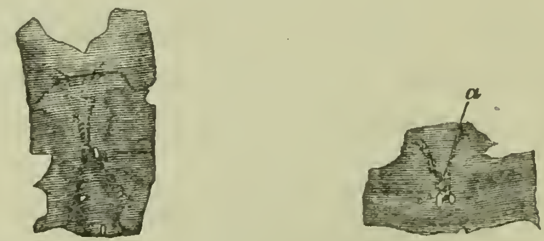
migration than of blood in bulk by rupture. An artery is sometimes remarkably fringed along its banks by defined

FIG. 2.

Blood corpuscles extruded from the vessels in case of early diabetes.

lines of extruded corpuscles, which are not accumulated as from a rent, but have a marginated arrangement along

FIG. 3.



The actual size and naked-eye appearance of the streaks of extravasation which are magnified in the adjoining cut. The streaks diverge on each side of the median line of the pons. The boat-shaped indentation left at the end of the larger section belongs to the fourth ventricle. The spot more highly magnified is indicated by the letter *a*.

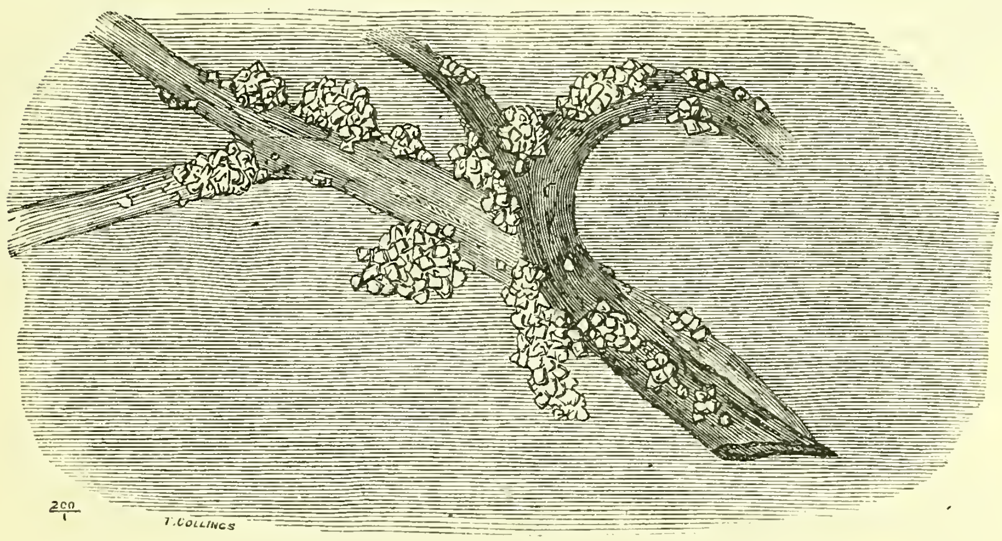
the turns and branchings of the vessel. The escape of corpuscles, however, can only be recognised in early cases. I traced it conclusively in a diabetic person who had died

at an early stage of the disease of an ailment apparently unconnected with it.

In this instance subsequent changes were anticipated by death. The next woodcut shows a later stage of extravasation. Nothing is left of the extruded blood but a mass of crystals of hæmatine, which are closely imbedded in the brain substance immediately outside the vessel from which the blood has issued. There is still no breaking down of tissue.

Where the disorder has run its course the cavities, which

FIG. 4.



Crystals of hæmatine, the remnants of extravasated blood, imbedded in the brain outside a vessel; from case of Kirby subsequently related.

are probably the sequelæ of such extravasations as have been described, are among its most conspicuous results. Sometimes these contain blood crystals in sufficient number to suggest a hæmorrhagic origin, while often such an origin can only be presumed by such collateral evidence as has been adduced.

When the disease has proceeded to its natural end the excavations are widely scattered through the brain; numerous, small, and closely set in the white matter of the convolutions, fewer and larger about the central parts. The corpora striata, optic thalami, pons, medulla, and cerebellum are the chosen seats for the largest and most striking

Place of excavations.

holes. In these situations the cavities are determined by the course of considerable arteries, or by penetrating folds of pia mater.

A common place for a conspicuous excavation is the centre of the pons Varolii at the tip of long process of pia mater which reaches in this direction. (Plate I. figs. 3, 4, and 7.) Cavities are often to be found on each side of the medulla oblongata in contact with the root of the facial nerve. (Plate II. figs. 3 and 4.) Others, smaller but scarcely less conspicuous, usually lie within and about the dentate bodies both of the medulla and cerebellum,

Fig. 5.

Erosions in the course of blood-vessels in the dentate body of the cerebellum. The arteries were in some instances much dilated.

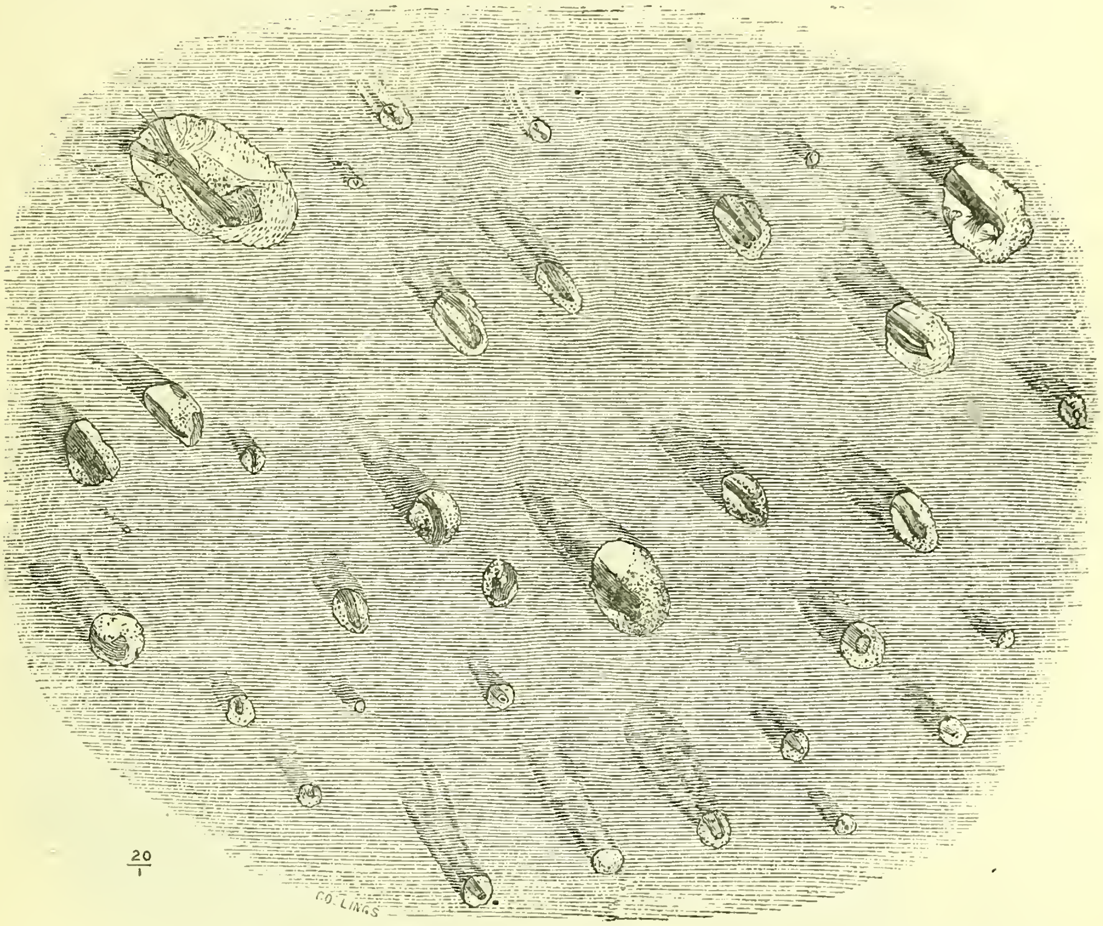
developed there in connection with the relatively large vessels which these centres receive. And many smaller punctures and tubular erosions are irregularly scattered through almost every part of the encephalon, the only limitation being that they are usually confined to the white matter. A striking instance has lately come under my observation (see case of Mackay), in which a large part of the optic thalamus was riddled with cavities of such size and so approximated as to liken it to volcanic lava or Gruyière cheese. The woodcut page 39 shows the cavities of their actual size.

In convolutions.

The white matter of the convolutions is often rendered strikingly cribriform, in patches, by numerous erosions. I have counted more than fifty within a space of not

half an inch square—minute, but distinctly visible to the naked eye. Each contains a vessel, usually an artery,

Fig. 6.



White matter of cerebral convolution showing change described, slightly magnified. The preparation was obtained from a case of chronic diabetes which is elsewhere fully related (Kirby). The affected spot might have been covered by half-a-crown.

around which is an irregular interval containing crystals of hæmatine and products of nervous degeneration. (Woodcut 6.)

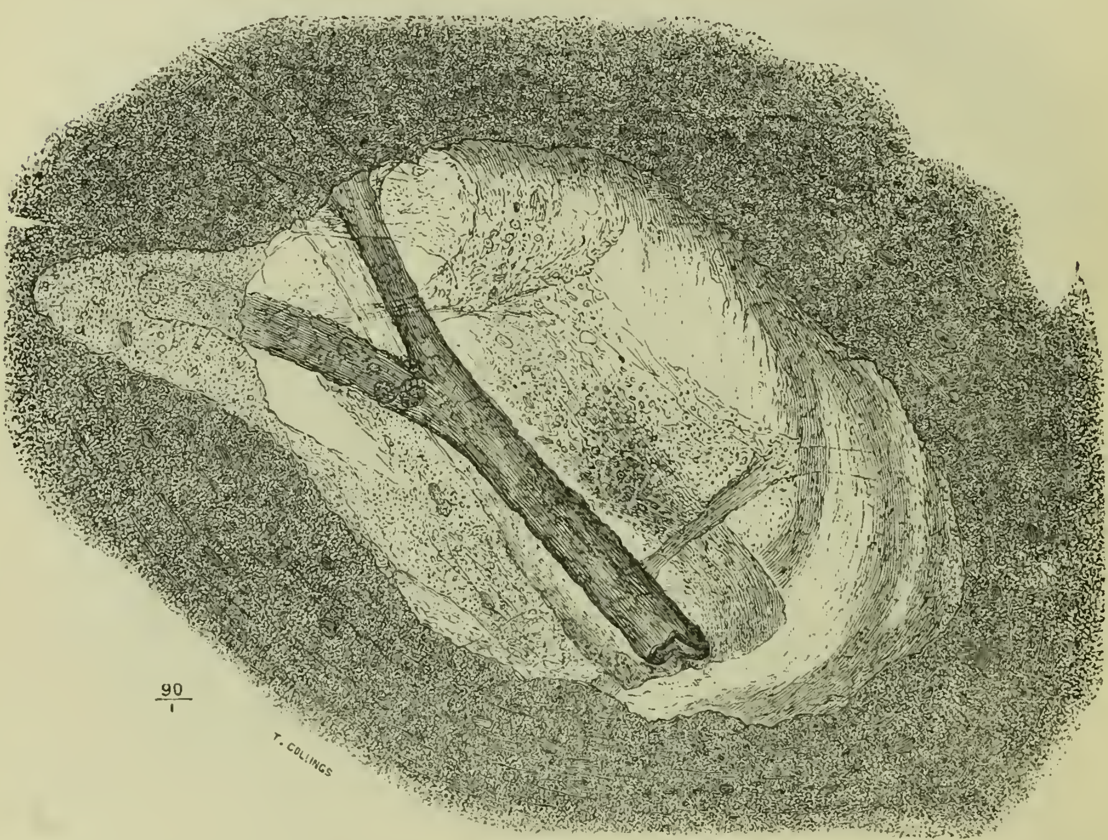
These holes are evidently exaggerations of the perivascular spaces.

The cavities, whatever their size and place, are much the same in appearance and contents. They are abruptly bounded, usually with a narrow margin of disintegrated nervous tissue, the brain matter outside this being absolutely natural. According to their date they contain degenerate remains of nerve tissue, remnants of blood

Their contents.

vessels or of extruded blood, or are empty. The products of nervous degeneration are first removed, then for a while the cavity contains only dilated or shrunken and obsolete arteries, with areolar tissue derived apparently from the

Fig. 7.



One of the excavations (that in the left-hand top corner in cut 6) more highly magnified. It is irregular in outline as if from erosion; while the contents are shreds and strands of nucleated areolar tissue, with which blood crystals are intermixed; the largest masses may be seen adhering to the artery near its bifurcation.

perivascular sheath, and crystals of hæmatine. Lastly these disappear also and a mere vacuity is left.

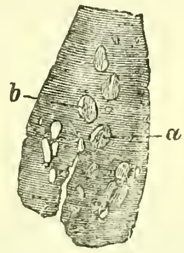
In rapidly fatal cases (Salisbury, Plate I. and Mackay, figs. 8, 9 and 10) the cavities, which in such are larger than when the disease has been more chronic, are sometimes filled with a translucent gelatinous substance containing besides vascular structure the granular or globular products of nervous disintegration, with delicate fibrillæ and nuclei derived in part from the peri-vascular sheath and apparently in part from the condensed re-

mains of the connective tissue of the destroyed nervous substance.

Fibro-nucleated material.

This transparent substitute for brain matter is soft, elastic, and often eludes the edge of the razor, so that

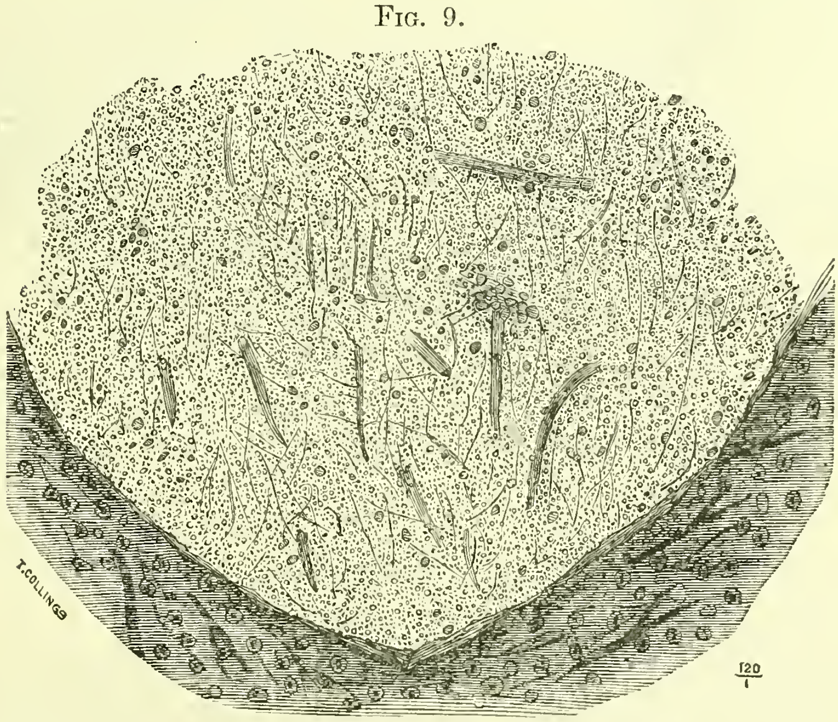
Fig. 8.



A section from the optic thalamus riddled with cavities of considerable size. Their actual dimensions are here given. From the case of Mackay in which the disease ran a very rapid course.
The letters *a* and *b* refer to the next cuts where the contents are shown.

though conspicuous enough to the naked eye it requires some care to obtain sections for the microscope. These when obtained present the appearances represented.

Fig. 9.



The contents of the cavity marked *b*, showing the translucent semigelatinous material exhibiting a delicate fibro-nucleated structure and containing the remains of blood-vessels. The edges are abrupt; the nervous structure natural up to the margin.

Vascular remains, nerve cells

Among the contents of such cavities it must be mentioned that large nerve cells displaced and somewhat

and blood crystals.

degenerated, are sometimes seen among the débris; as if such cells, the place of which had been usurped by the excavation, survived the destructive process longer than the nerve fibre.

In the more chronic form of the disease, as it occurs in elderly persons, the excavations are usually empty, though the remnants of nervous decay are usually to be found

FIG. 10.

Contents of the cavity marked *a*; contorted and entangled vessels, chiefly arterial, fibro-nucleated tissue, large, displaced, and scattered nerve cells, and crystals of hæmatine.

fringing their margins, or collected as an irregular sheath upon the dilated or shrunken artery.

The changes in the cord are similar to those in the brain but less declared. Erosions about the arteries are evident especially in the transverse commissure, the white band of which is sometimes completely divided in the track of one of its large vessels. Holes such as have been described in the brain sometimes though rarely perforate the grey horns. The most striking change in the cord,

To face plate 1, *page* 40].

DESCRIPTION OF PLATE I.[1]

SECTIONS OF BRAIN FROM DIABETIC SUBJECTS.

Figs. 1, 2, and 3 relate to the brain of a boy named Hatcher, who died at the age of six years, having had the disease for six months. It was marked by severe symptoms, the urine having a specific gravity of 1056 ; the temperature of the body falling as low as 93·6. The immediate cause of death was inflammatory œdema of the lungs. The case is related at length in the *Medico-Chirurgical Transactions* for 1870.

Fig. 1.—An oval cavity at the lowest part of the medulla close to the central canal. Shown of the natural size, and also magnified 150 diameters.

Fig. 2.—An excavation around an artery in the central part of the olivary body. The artery is covered with the products of nervous degeneration. Magnified 150 diameters.

Fig. 3.—A large excavation in the anterior part of the pons Varolii. Shown of the natural size, and also magnified 4 diameters.

(Further illustrations of this case are given in Plate II.)

Figs. 4 to 7 relate to the brain of a man named Salisbury, who died of diabetes at the age of 25, having had it apparently for about nine months. The most striking feature in the case was the enormous production of sugar and diuresis. He passed in one day more than 50 ounces of sugar and 532 ounces, or more than 26 imperial pints, of urine. His diet was at this time without restriction. It was afterwards limited, with a great reduction both of the sugar and of the amount of urine ; but the man, impatient of the restraint, left the hospital, resumed his former indiscriminate diet, and shortly afterwards fell into a state of coma, in which he died.

The case is given in detail in the *Medico-Chirurgical Transactions* for 1870.

Fig. 4.—An excavation in front of the pons. Natural size.

Fig. 5.—A cavity around a dilated blood-vessel in the grey matter near the floor of the fourth ventricle. Of the natural size, and magnified 50 diameters.

Fig. 6.—Cavity at the root of the facial nerve. Natural size.

Fig. 7.—Cavity in the median line near the front of the pons, containing arteries and nervous detritus. Natural size, and magnified 50 diameters.

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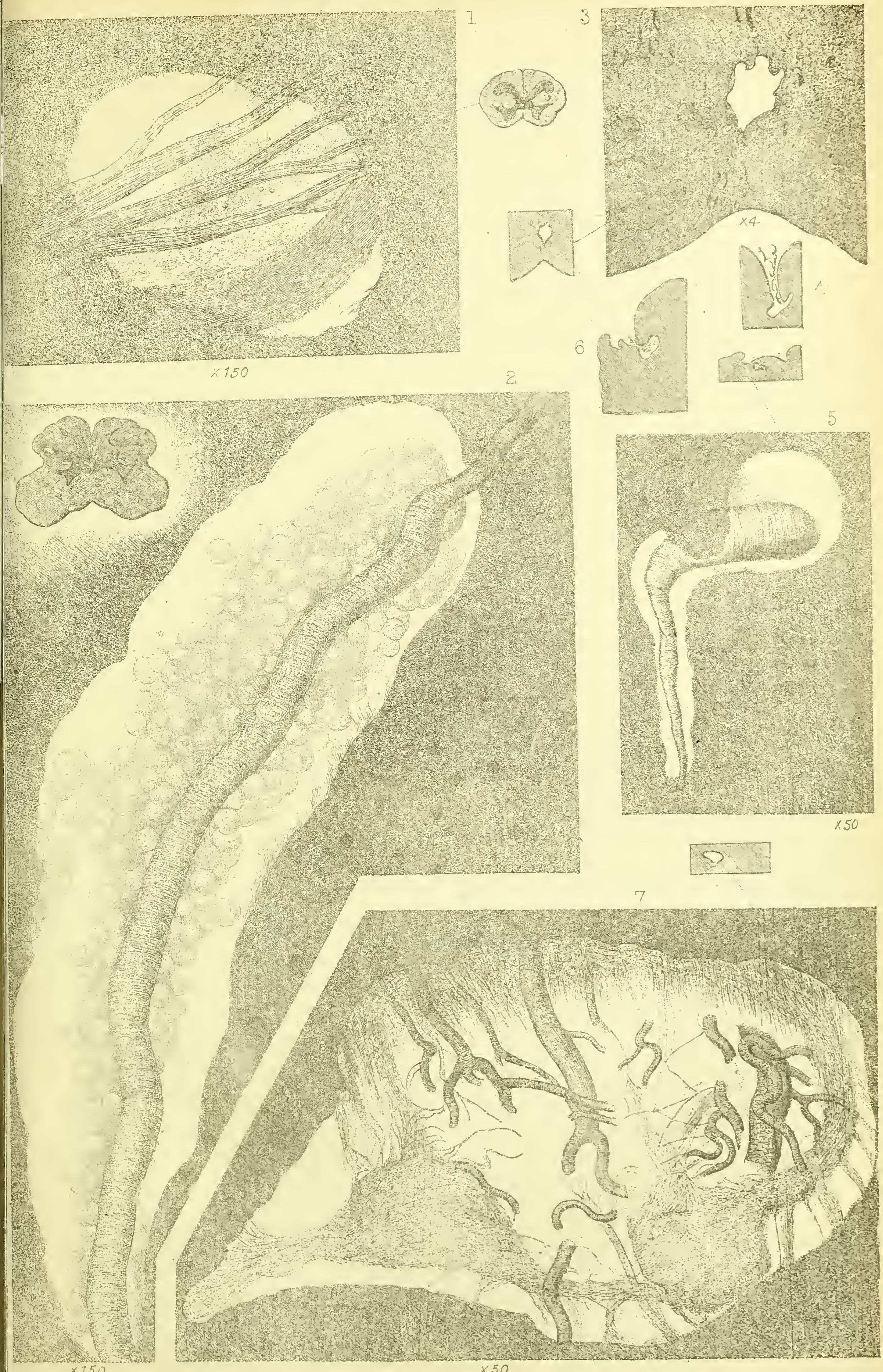
[1] I am indebted to the Medico-Chirurgical Society for permission to reproduce Plates I. and II., which originally illustrated a paper in its *Transactions.*

Plate. I



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To face plate 2, page 40].

DESCRIPTION OF PLATE II.

SECTIONS OF BRAIN AND CORD FROM DIABETIC SUBJECTS.

Figs. 1 and 2 relate to the brain of a man named Passenger, who died in a state of diabetic coma at the age of 23. He had had the complaint for two years and three months. (See *Med.-Chir. Trans.* for 1870.)

Fig. 1.—A cavity around an artery opposite the decussation in the lowest part of the medulla. Of the natural size, and magnified 50 diameters.

Fig. 2.—Cavity around an artery in the white matter of the olivary body, edged with broken-down tissue. Of the natural size, and magnified 50 diameters.

Figs. 3 and 4 represent the morbid appearances in the pons Varolii of Hatcher, other portions of whose brain are represented in Plate I. It may be stated that the large hole at the root of the facial nerve which the two figures referred to represent was just as conspicuous to the naked eye as with the microscope.

Fig. 3.—A section of the posterior part of the pons Varolii of the natural size. It shows the excavation at the root of the facial nerve.

Fig. 4.—The cavity at the root of the facial nerve magnified 20 diameters. The broken vessels are seen protruding from the wall. The root of the nerve is seen close to the end of the cavity.

Figs. 5 to 8 represent the morbid appearances in the brain and cord of Sarah Stewart, who, while under opium, fell into a state of diabetic coma, and so died, at the age of 26, having been the subject of diabetes for about twelve months. Perhaps the most striking of these were the holes which so closely beset the white matter of one of the convolutions that the affected patch had a cribriform look, evident to the naked eye and in the fresh state, as if it had been designedly punctured with a thick pin. These are represented in Figs. 7 and 8. It may be added that the liver represented at page 49, and the lung at page 55, were obtained from the same subject.

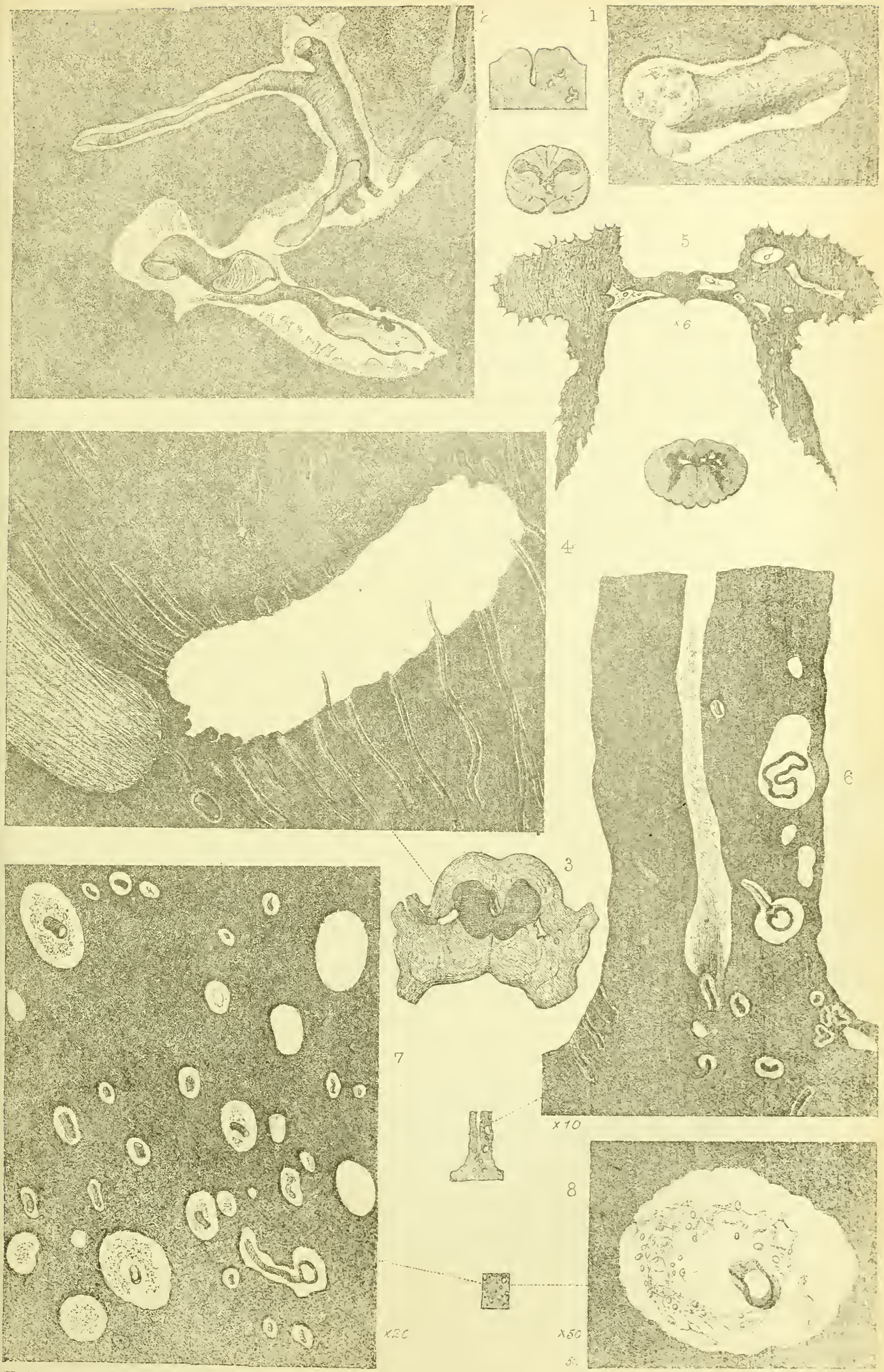
Fig. 5.—The grey matter of the spinal cord in the cervical region, showing considerable excavations in the commissure and the lateral grey matter. Of the natural size, and magnified 4 diameters.

Fig. 6.—A transverse action of the septum of the ventricles, showing large excavations about its blood-vessels. Of the natural size, and magnified 6 diameters.

Fig. 7.—The white matter of a cerebral convolution, showing numerous cavities, some containing blood-vessels. Of the natural size, and magnified 20 diameters.

Fig. 8.—One of the cavities in Fig. 7 magnified 50 diameters, showing a loose web containing grains of pigment around the vessel, presumed to be an altered condition of the perivascular sheath.

Plate II.



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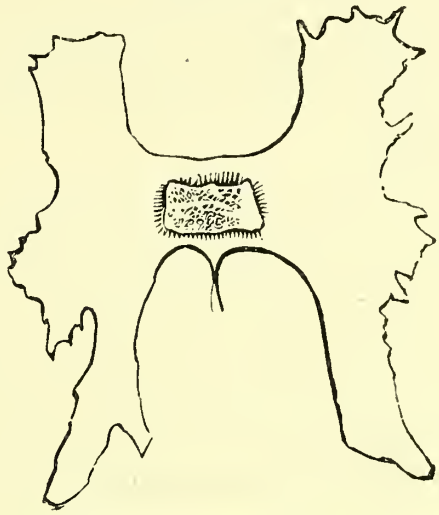
however, is dilatation of the central canal, which in the dorsal and lumbar regions is sometimes expanded to many

Enlargement of central canal.

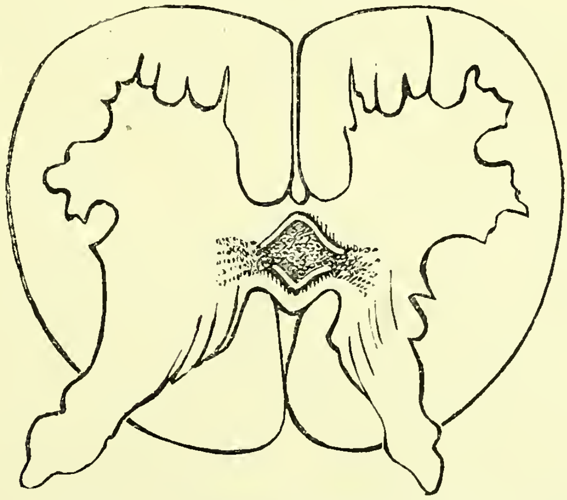
Fig. 11.



Enlargement of the central canal of the cord in the dorsal region to $\frac{1}{24}$th of an inch in width. The space contained a small quantity of granular matter. From a case of diabetes in a man 32 years of age reported in the 'Med.-Chir. Trans.' for 1870, p. 18.

times its normal diameter, and forms a conspicuous object immediately the cord is divided. This expansion of the

Fig. 12.



Enlargement of the central canal in the lumbar region, from a man 39 years of age. The canal measured $\frac{1}{27}$ of an inch transversely, it was filled with granular matter which passed into, and issued from, the grey horns at each lateral corner of the canal. From 'Med.-Chir. Trans.' 1870, p. 24.

channel is not constantly present, but when it is, it is sufficiently remarkable. I am not aware at present how

far it is peculiar to diabetes. The annexed outlines, drawn with the camera lucida, show the relative size of the canal as compared with the grey columns. The cavity is occupied by granular products which appear to be derived in part at least from an overgrowth of the epithelium lining it, which is sometimes in these cases in a state of active and irregular proliferation.

Miliary sclerosis.

This sketch of the morbid anatomy of the nervous system in diabetes would be incomplete without mention of a single case, in which, in addition to the changes described, I found throughout the white matter of the brain and cord the peculiar form of disseminated degeneration which has been described as miliary sclerosis. The case was that of a young woman who died of diabetes at the age of 18.[1]

I am indebted to Dr. Thorowgood, under whose care she was, for the opportunity of examining the nervous centres.

First as to the encephalon, the white matter here was generally dotted with smooth specks which were distinguished from it by their more absolute whiteness. These though always minute were mostly evident to the naked eye. Their general shape was ovoid or elongated. The larger measured about $\frac{1}{30}$th of an inch in their longer, $\frac{1}{50}$th in their shorter diameter. The smaller had about a tenth of those dimensions, and could not be discerned but with the microscope. Within these spots, which were generally gradually shaded into the surrounding tissue, though some, especially the smaller, were sharply circumscribed, the nerve fibres were entirely replaced by a structureless or dimly globulated material (Plate III.) which appeared to be disintegrated nervous matter. These specks of degeneration had a dead white or faint greenish tinge and absolutely refused carmine, so that this pigment, tinting the surrounding tissue with its wonted pink, marked their

[1] A description of miliary sclerosis may be seen in a paper by Dr. Batty Tuke in the 'British and Foreign Medico-Chir. Review' for July, 1873, and another by Mr. Kesteven in the same periodical for July 1874.

To face plate 3, page 42].

DESCRIPTION OF PLATE III.

MILIARY SCLEROSIS ASSOCIATED WITH DIABETES.

The patches of sclerosis found in the case referred to at page 42—rather accidental complications of diabetes than properly belonging to it.

The peculiarities of this case may be briefly summed up in the occurrence, in addition to the perivascular changes which are proper to diabetes, of an universal besprinkling of the nervous centres by a grey degeneration not immediately dependent on the position of the blood-vessels.

Fig. 1.—Section of cord from the dorsal region, showing a spot of translucent disorganisation in the midst of each anterior horn. The white matter of the cord is dotted with so-called corpora amylacea and miliary spots of sclerosis, such as are found in the brain, though with the low power used in magnifying this section they can be scarcely distinguished.

Figs. 2, 3, and 4.—Miliary spots of degenerated white matter or sclerosis from different parts of the brain ; Fig. 2 from the mesocephale, near the median line ; 3, from the trunk of the arbor vitæ ; 4, from the white matter of one of the cerebral convolutions. The spot from the arbor vitæ is more distinctly globulated than the rest, giving the kind of structure which degenerated white matter assumes in many circumstances. Corpora amylacea were scattered in the neighbourhood.

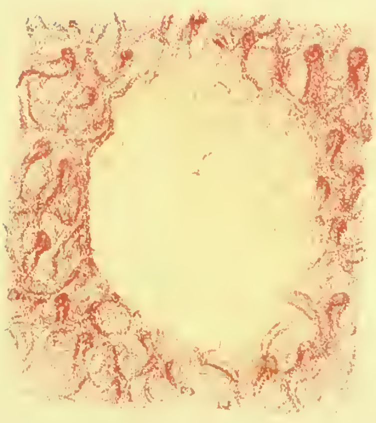
Fig. 5.—In the same region—the central white matter of the cerebellum—were some dilated vessels, which, from the thinness of their walls, were apparently small veins, much stretched. They were empty of blood, but contained sharply outlined bodies, which, however produced, resembled the smaller corpora amylacea which were so frequent in the white matter. One of these corpora amylacea may be seen partially overlying the dilated vessel.

Plate III

1

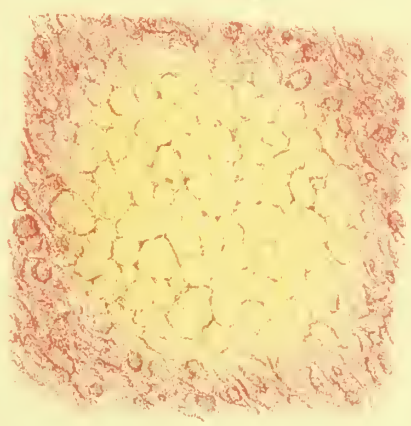
× 15

2



× 200

3



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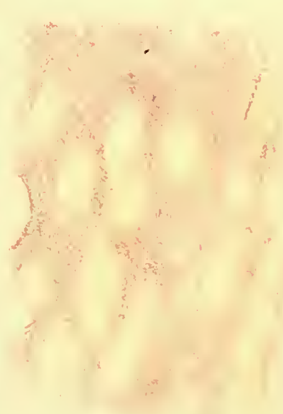
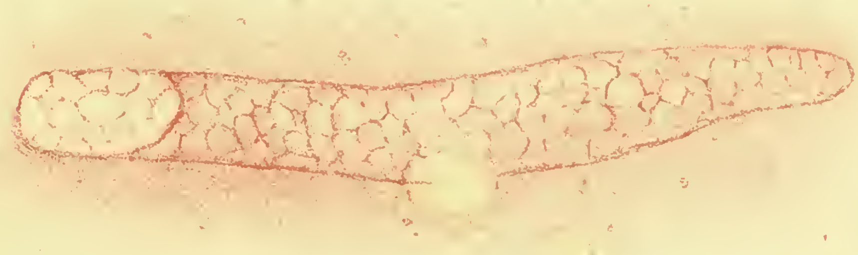


× 15

5



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presence with exceeding distinctness. No part of the white matter was entirely free from them. Many were found in the cerebral convolutions. But they were most numerous in the pons medulla and cerebellum. In the arbor vitæ I counted within a space a quarter of an inch square as many as 40. Elsewhere they were less numerous. No relation could be traced between them and any vascular structures, and it does not appear that the change can be more definitely described than as a speckled degeneration of the white matter.

The spinal cord presented changes as striking. I need not describe the excavated channels in the grey horns; such evidences of perivascular destruction as were found in the other cases were conspicuous in the cord as well as in the brain of this subject.

With reference to the peculiar speckled degeneration, the spots were thickly scattered through the white matter of the whole cord; they were generally smaller than in the brain, the larger being caused by a confluence of several. Some were within the range of the naked eye, most not. In colour, translucency, and structure the description of the spots in the brain exactly applies. (Plate III.)

In the grey matter of the dorsal region was a change not less remarkable. A rounded patch of bright translucency occupied the central part of each anterior horn. The peculiar glassy transparency, nearly symmetrically placed on the two sides, was striking to the naked eye. The vitrified spot, if I may use such a simile, consisted of coarsely crumbled matter (Plate III.), probably the product of nervous degeneration, intermixed with waving fibres of areolar tissue. Greatly dilated arteries could in some instances be traced across the affected spot. In the lumbar region were a few incipient spots of the same kind.

It should be mentioned that many of the affected spots, particularly in the grey horns, contained numerous crystals which, from their solubility in ether and their reaction with iodine and sulphuric acid, appeared to be cholesterine.

Their presence at first inclined me to the belief that the miliary changes were due, as probably were the crystals, to the action of the alcohol, but further consideration has led me to concur with the view maintained by Mr. Kesteven that the changes are of morbid origin.

The pathological relations of *disseminated sclerosis*, as it has been termed, are somewhat indefinite. The miliary spots in the present instance gave no evidence of induration or connective hypertrophy, but were merely patches of white fibres whose material had fallen, as is usual with degenerating white fibres, into a globulated shape and structure. This change has been found in so great a variety of nervous affections that it can scarcely be regarded as evidence of anything more specific than destruction of fibre, widely scattered but nowhere extensive. This probably may take its rise in many morbid states. The fact that it was found in this instance only of eleven, shows that it is not essential to diabetes, as are the perivascular changes which are constantly present, and were typically so in this instance.

Considerations upon the nature of the nervous lesions.

No question can be raised as to the concurrence with diabetes of the changes which have been described. It only remains for consideration whether the glycosuria causes the cerebral lesions, or the cerebral lesions the glycosuria.

Is it possible that the erosion and perivascular destruction should be due to the action of the saccharine blood upon the delicate nervous tissue? The handling of sugar causes grocers' itch; the contact of diabetic urine causes eczema; in diabetes the lung, and to a less extent the kidney, takes on inflammatory action: may not the nervous changes, more especially as they follow the course of blood-vessels, be attributed solely to the morbid influence of the diabetic blood? This hypothesis at first sight seems not improbable, but looked at more narrowly we cannot but discern considerations which make against it. Diabetic blood is not generally irritating to the tissues. The

absence of atheroma and vascular degeneration is as striking in diabetes as is their presence in albuminuria. The tubal disturbance of the kidney is probably no more than the diuresis is sufficient to explain ; and the pulmonary change, however it may arise, is especial to the lung rather than concurrent with similar changes elsewhere. And it is also contradicted by the limitation of changes to the course of the arteries. If the destruction were wrought by a circulating agent, it would probably show itself rather in the territory of the capillaries, where the blood is brought into its most intimate relation with the tissues, than about the arteries, where it is divided from them by thick walls. Besides this the process by which, as far as we can see, the excavations are produced—and specimens at different stages of the disease enable us to trace this with some clearness—points to an alteration, not in the quality, but in the distribution of the blood as the first step. Localised loss of arterial tension, repletion of the affected trunks, consequent serous leakage or corpuscular migration, and finally disintegration and removal of the permeated tissue, appear to constitute the alterations of diabetes as of other diseases of the nervous centres. For this mode of nervous failure is common to many disorders, and according to its situation and intensity may give rise to different symptoms and be known by different names.

From the place and character, therefore, of the nervous lesions of diabetes we may infer that they are not due to the presence of sugar or to any other peculiarity of diabetic blood, and are probably not to be regarded in any way as results of the disease, but are original to the nervous system and constitute the initial fact of the disorder of which glycosuria is the leading symptom. This view of the nervous, or it may be said of the cerebral, origin of the disease is remarkably confirmed by the common experience that the most frequent, or I may say the only surely recognised, causes of diabetes—putting aside accident and hereditary tendency—are mental.

The lesions of diabetes are characteristic of their

nervous origin in their resemblance to those of tetanus and general paresis, from which they differ in disposition, date and degree, and not in kind further than that with general paresis cellular degenerations are superadded.

Every tissue has its own way of behaving under disease. Under the same influence, say of hyperæmia, one tissue may indurate, another soften, a third caseate, a fourth dissolve and disappear. Fibrous tissue thickens and indurates; muscle becomes fatty and softens; pulmonary tissue hepatizes, caseates, disintegrates, and finally is spat up; nervous matter softens and, if death do not interfere, melts away and is removed by absorption, leaving simple vacuities as the only record of the morbid process.

Vacuolation in its pathological relations.

Vacuolation may be found in nervous tissue probably from as many different conditions as give rise in the lung to caseation. The vacuoles of diabetes present a mode of decay which nervous matter may in many circumstances present, so long as they are accompanied with the forcible extrusion without rupture of blood or one of its components. Thus there are many diseases of the brain and cord in which disintegration, erosion, or excavation are found—to wit such chronic changes as produce insanity, more especially general paresis, the lesions of which are, as has been stated, nearly akin to those of diabetes. Whether the symptoms shall be those of one disease or another may depend on the position, degree, and complications of the change.

The changes described as of diabetes point significantly to the symptoms observed; glycosuria resulting, as has already been shown, from nervous irritation rather than from loss or interruption of nervous power. They are records of degeneration, not uniformly throughout the brain, but at numerous and widely scattered points which are sources of irritation rather than evidences of potential loss of material. The changes though widely disseminated are not evenly diffused. The nerve cells remain natural up to the very edges of the excavations. The alterations are limited to the white matter, and even there

no considerable tracts of fibres are severed so as to occasion, or to lead one to expect, paralytic results.

Liver.

As the brain is the agent, the liver is the instrument, of glycosuria. The brain misguides the liver, the liver misappropriates the nutriment. Secondly, to the changes in the nervous centres those which the liver presents may be taken into consideration. We find alterations in its tissues which cannot generally be considered as prime causes of diabetes, but which concur with altered or excessive function.

Congestion and cirrhosis.

Prout, a most accurate observer, noticed as a general sequence of death by diabetes a gorged condition of the veins terminating in the portal system; and noted 'hepatic disease or disorder' among the earlier complications of the complaint in question. He instances chronic inflammation with congestive enlargement and jaundice, and 'too frequently organic disease,' as associates of diabetes. Andral observed hyperæmia of the liver in the same circumstances. Trousseau drew attention, as connected with diabetes, to *hypertrophic cirrhosis*, that is, cirrhosis with enough overgrowth of the fibrous elements to give unevenness of surface, but also characterised by an increase in the epithelial or secreting portion such as to cause general enlargement of the organ. Later observers also have noticed hepatic changes in diabetic subjects. Dr. Wilks has noted that the diabetic liver is dark, tough, and homogeneous; and no one who has often seen the post-mortem examination of diabetic persons can fail to have observed general signs of increased vascularity, depth of colour, and unnaturally firm consistence as especially belonging to the disorder. The bile is generally yellow or rhubarb-tinted, or, according to Dr. Pavy, red or brownish-red, with a deposit after standing of epithelium and granular matter.

Bile.

Referring to the post-mortem records of St. George's

Post-mortem details.

Hospital, I find 27 instances including some which I have elsewhere given in detail, in which the condition of the liver in diabetes has been described. This organ was natural in 6 only. In 13 various degrees of congestion were noted, sometimes without obvious change beyond superabundance of blood, sometimes associated with increase of bulk, hardness of tissue, or fatty change. In one instance the hyperæmia was shared by the veins of the omentum and mesentery; in another it had given rise to extravasation in the glandular tissue; in two it was accompanied with coagulation which had taken place during life chiefly in the portal channels of the organ; and in an exceptional instance there existed the remarkable patches of capillary dilatation to be presently described.

Fatty change was noticed altogether in 7 instances; 3 were found in which the bulk or consistence of the organ were increased without other apparent change; while one case was a striking example of what has been termed hypertrophic cirrhosis, the organ displaying marked increase of fibroid tissue and nodulation of surface, and weighing more than 9 pounds.

The annexed table shows in detail the state of the liver in each of the 27 cases alluded to.

Condition of Liver in 27 Cases of Saccharine Diabetes.

	Cases.
Healthy in	6
Congested in	4
Intensely congested in	1
Intensely congested, as also were veins of mesentery and omentum, in	1
Highly congested, hard or tough	3
Highly congested, with fatty change	1
Highly congested, with extravasation and fatty change	1
Highly congested, with coagulation in veins and fatty change	1
Highly congested, with coagulation in veins and peculiar capillary dilatation	1
Fatty	1
Fatty and enlarged	3
Enlarged or hard without other change	3
Weighed 9 lbs. 2 oz. Hard, yellow, granulated (cirrhosis)	1
	27

On microscopic examination of the diabetic liver overgrowth and crowding of the epithelium is often to be seen, along with frequent evidences of hyperæmia. In two cases elsewhere referred to, extensive districts of the

Coagulation in the vessels.

FIG. 13.

A portal canal containing two branches of the portal vein filled with ante-mortem clot. The adjacent branches of the hepatic artery are similarly occupied. All the blood-vessels distinguishable in the neighbouring glandular tissue are likewise obstructed. (From case of Stewart, see plate II.)

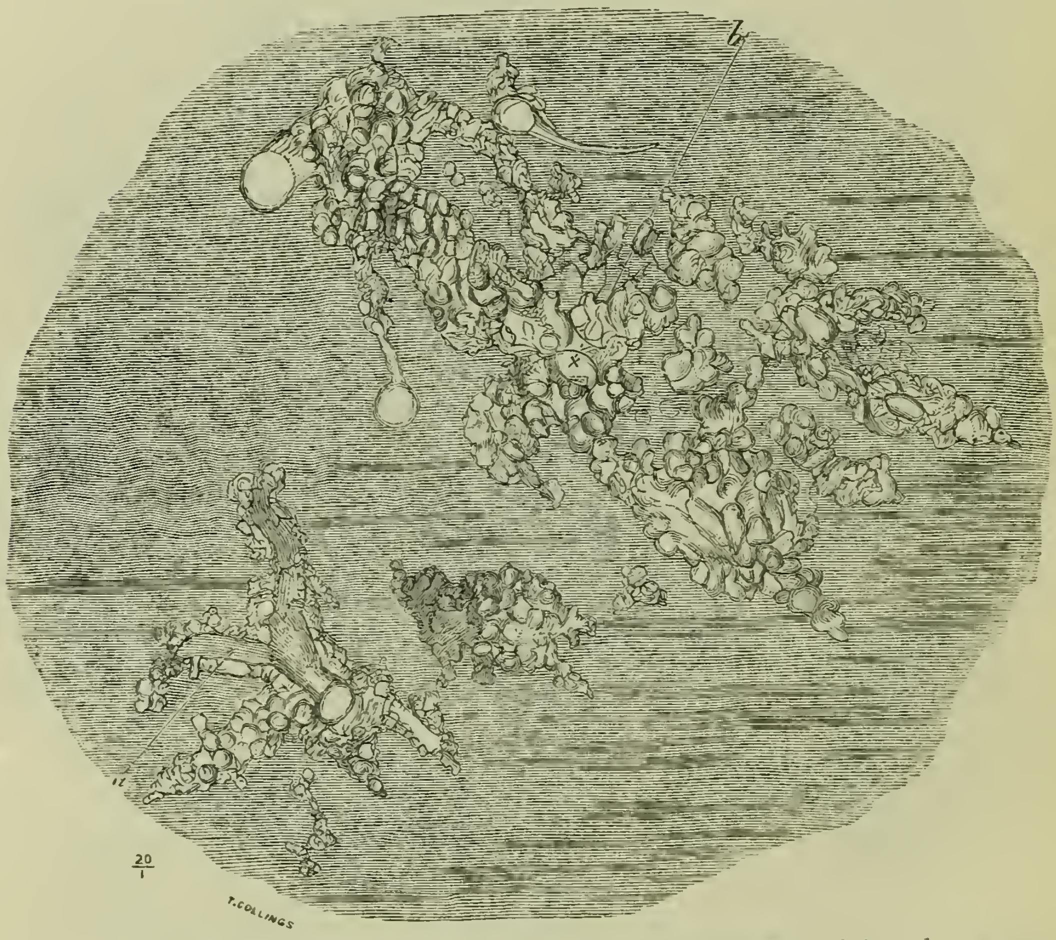
portal vein were occupied by coagulum, which, by the changes it had undergone, had manifestly formed there in life. In one instance it ramified minutely, reaching even into the small interlobular branches of the portal vein, and

fewer clots were also formed in the neighbouring divisions of the hepatic vein and artery. The condition of the vessels is displayed in the annexed woodcut.

Dilatation of capillaries.

In one instance, and in one only, so that what I am about to describe forms no part of the necessary anatomy of diabetes, though of interest in connection with the other changes, I found in addition to general venous thrombosis,

Fig. 14.



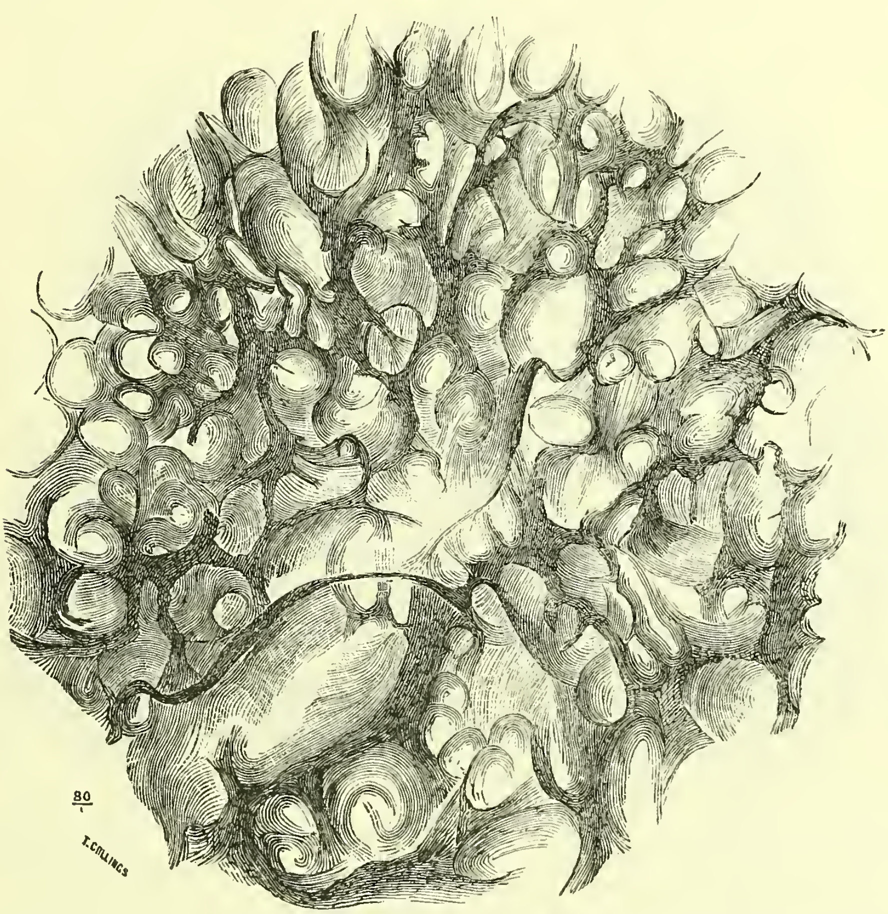
Patches of capillary dilatation as seen under a low power, giving the worm-eaten effect. *a* indicates the position of a considerable branch of the hepatic vein.

and apparently in connection with it, patches of a remarkable spongy transformation, which I was at a loss to explain until I obtained the clue from my friend Dr. Lionel Beale. They proved to be caused by an extravagant dilatation of the capillaries belonging to the hepatic vein.

Patches of liver substance—that to which the accompanying illustrations relate was about as large as a shilling

—had a closely dotted or dark stippled texture and an elastic softness quite different from the surrounding tissue. Under the microscope sections from the affected region had a worm-eaten or honey-combed look; the dense hepatic tissue being patched by an open network the strands of which were as slender in relation to the spaces as are the septa of a honey-comb. The threads of the

Fig. 15.

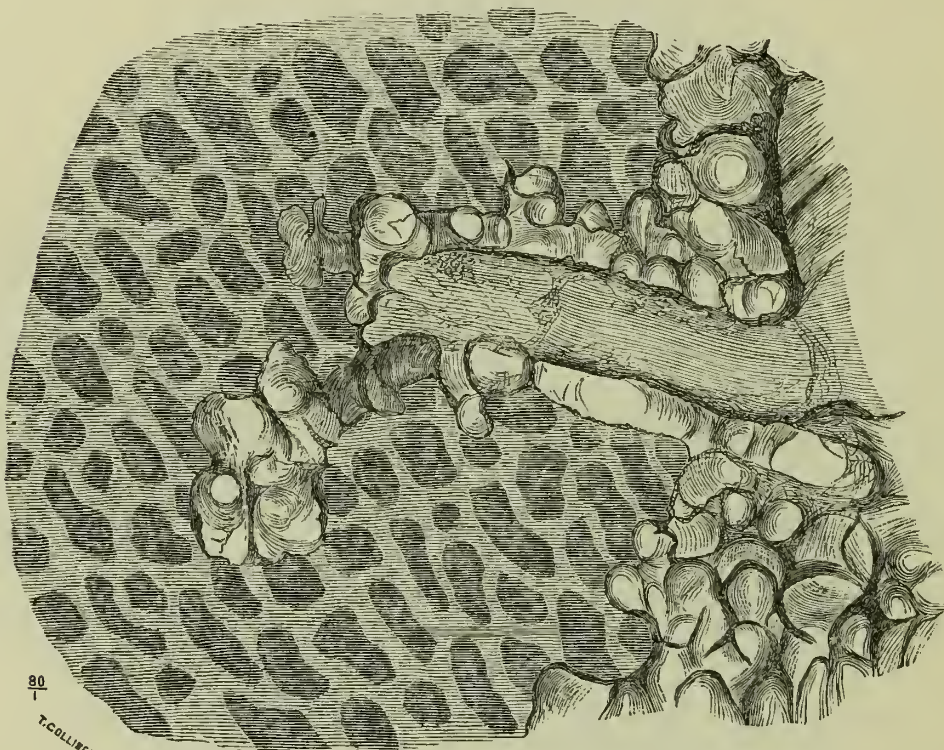


The portion of the patch marked *b* more highly magnified, showing the openness of the network and the total transformation of the hepatic structure.

network were chiefly of glandular epithelium compressed and elongated; the cavities were empty and proved to be those of contorted tubes, the cellular appearance being a somewhat delusive result of section. The tubes in many instances distinctly opened into branches of the hepatic vein, and in short the whole mass of spongy transformation appeared to be due to a partial but extravagant dilatation of the capillaries in connection with this venous

channel. The stretched capillaries often followed in marginal arrangement the course of a hepatic venule, or encircled one of the larger trunks as seen in section. The dilatation was such as to compress almost to extinction the intervening glandular structures. The affected capillaries were about twice the width of the lines of natural epithelium forming the acini. The dilated capillaries were uniformly empty, though coagulum

Fig. 16.



The hepatic venule marked *a*, and its neighbourhood more highly magnified The dilatations are seen following the course of the vein and communicating with its cavity. The mottled shading indicates natural hepatic tissue.

evidently of old date was found in some of the venous radicles with which they were in connection. The fact that in many instances the expanded capillaries could be distinctly traced as tributaries of hepatic venous branchlets, which were obstructed by ancient coagulum, suggested occlusion of the vein of exit thus wrought, as the cause of the dilatation. The steps of the process in this view would be closure by clot of the hepatic venule; distension and dilatation of the capillaries opening into it; closure by clot

of the portal branch supplying them; removal by absorption of the blood or clot in the distended capillaries, leaving a network of empty stretched vessels, into which no blood enters.[1]

Summary of hepatic changes.

The peculiarities of the diabetic liver may be generally summed up as increase of blood and such changes in its tissue as chronic hyperæmia induces—enlargement, hardness, and overgrowth of epithelium and fibrous tissue. The alterations in this organ are such as consort with the view that it is not primarily affected in this disease, but that it is modified by an over-activity of circulation and function which is instigated by influences external to itself.

Lungs.

Pulmonary changes regarded as phthisical or tuberculous have long been known as apt to follow upon diabetes. Until recently no distinction has been made between these alterations and those of ordinary tubercular consumption. Dr. Wilks, however, and his colleague Dr. Pavy, have recognised the disease of the lung which ensues upon diabetes as of inflammatory origin and as essentially different from that set up by tubercle, though resembling it in its course and results.

The lungs of diabetic subjects are seldom natural; in a large proportion of cases disease of these organs causes or heavily contributes to the fatal end. Hepatisation, caseation, and excavation are common. The changes though often simulative of tubercle are not tubercular. Diabetic patients, indeed, appear to have an exceptional immunity from that formation; or to say the least, are so seldom the subjects of general tuberculosis that we may safely infer that there is no pathological connection

[1] These peculiar changes were found only in one subject (see case of Kirby, subsequently related). They cannot be supposed to be essential to the disease, though they are illustrative of its process. They have been placed in this general sketch of the pathology of the disease, chiefly for the sake of having all the drawings of morbid appearances together.

between tubercle and diabetes. Twenty-seven post-mortem examinations of diabetic subjects at St. George's Hospital gave no instance in which tubercle-like changes were found elsewhere than in the lung, save in a single instance in which a cheesy mass surrounded by a fibrous capsule existed in one kidney—general or scattered tuberculosis was unrepresented in the series. The following table gives the results alluded to.

State of the Lungs in 27 *Diabetic Subjects examined at St. George's Hospital between the years* 1842 *and* 1873.

Total number of examinations	27
Lungs healthy in	2
Congestion in	9
Serous infiltration or œdema in	7
Red hepatisation in	1
Grey hepatisation, breaking down, in	2
Sloughy cavities in	2
Cheesy or 'yellow scrofulous' masses. sometimes suppurating in	13
Cretaceous mass in bronchial glands in	1
Miliary or grey tubercle in	3
Vomicæ in	9
Tuberculosis, general throughout body, in	0

Rarity of true tubercle.

The rarity of the typical grey tubercle is striking. The destructive process to which the lungs in these circumstances are especially prone, appears to be a variety of pneumonia—chronic, circumscribed, and caseating—which rapidly leads to the formation of cavities. It is not easy with the naked eye to distinguish the caseous nodules, which thus result from those which belong to tubercular disease. Their non-tubercular origin may, however, be inferred from the general absence of formation, especially characteristic of tubercle, of grey granulation in the lung, and of tubercle-like growths in other organs.

The cheesy deposits of diabetes differ from those of tubercular origin also in their more rapid excavation; and it may perhaps be mentioned as another point of difference that the former are especially prone to occur at the lower part of the upper lobe, while tubercular disease more often chooses the apex.

With diabetes inflammatory affections of the lung of every kind occur, not necessarily as due to influences from without, but as part of the course of the disease. Red and grey hepatisation are found, the latter tending early to breaking down and to the formation of sloughing cavities.

FIG. 17.

Patch of circumscribed excavating pneumonia from case of diabetes (Stewart, plate II). The air cells are generally filled with corpuscular formation. A small cavity was formed in the centre; traces of lining membrane may be seen upon the walls. Pigment is seen about the blood-vessels and fibrous tissue.

MICROSCOPIC APPEARANCES IN THE LUNG.

The microscope shows the tubercle-like nodules of diabetes to be due to a form of circumscribed caseating pneumonia. Nothing of a definitely tubercular character

can be discovered. The air cells which are the especial seats of the exudation are occupied by a corpuscular product which cannot be distinguished from that of ordinary chronic pneumonia. The interalveolar septa in the affected parts often break down, so that many cells are thrown into one, thus giving rise to vomicæ sometimes of considerable size. The excavating process appears to be due simply to the softening of pneumonic products with consequent breaking down of the air cells in which they have been included. The resemblance of the change to tubercular phthisis lies only in the limitation of the process to certain districts of pulmonary tissue.

Excavating pneumonia.

Within the affected parts the fibroid septa of the lung are thickened, and a further result of chronic inflammation is to be found in marked pigmentation about the blood vessels of the regions involved in the morbid process.

Change probably of nervous origin.

The origin of the pneumonic change in diabetes has been ascribed to the contact of saccharine blood. Dr. Pavy, indeed, has expressed an opinion that if the sugar in the blood is kept down by treatment the susceptibility in question no longer exists. I have, however, found caseous masses and cavities where the diabetic restriction as to diet has been long and fully enforced ; and it would seem improbable that saccharine blood should act as an irritant upon the lung while upon other organs it has no such effect. Local inflammations do not occur in diabetes as with albuminuria.

In diabetes the blood-vessels do not become atheromatous or the heart hypertrophied ; nor can any general inflammatory tendency be traced. The lung change may with more probability be referred to the nervous system, and attributed to an influence locally directed rather than to one which with the blood would be impartially distributed.

Pneumonia and pleurisy result from many injuries of nervous structures. Dr. John Reid[1] refers to the frequent occurrence of pneumonia in his experimental

[1] Reid's 'Physiological Researches,' p. 143.

sections of the pneumogastric nerve. Brown Sequard[1] found that pneumonia, extravasation of blood into the pulmonary tissue, and bronchial effusion resulted from injuries of the brain, especially such as implicated the pons Varolii. Dr. Pavy[2] ascertained pleurisy to be a constant result of section of the sympathetic cord immediately above the superior thoracic ganglion. And this observation has especial interest in the circumstances under discussion, since we may suppose that with the lung as with the liver the morbid influence is conveyed, in the later part of its course at least, by the sympathetic filaments. Looking as we must at the altered function of the liver in diabetes as due to nervous hyperæmia originating in cerebral irritation directed to the gland ultimately by the sympathetic nerve, we may with much probability assign the state of the lung to a similar result of the same central influence.

It would seem that in morbid conditions apart from diabetes the vascular state of the lung is swayed by cerebral impressions. Many cases suggest that the development of tubercular phthisis under mental distress may be the result of a morbid nervous impression directed primarily upon the lung rather than a mere localisation of a tubercular tendency produced by general impairment of nutrition. The lung may be affected solely and so early that the impairment of health must be traced to the organic lesion rather than the organic lesion to the state of health.

Kidneys.

Diabetes, though not produced by any renal changes, is often associated with renal disturbance. The increased urinary flow necessitated by the disorder gives rise to congestive changes in the kidney resulting from the abnormal demand upon its function. The kidney is usually found to be bulky and more than naturally full of blood. Placing

[1] 'Lancet,' 1871, p. 6. [2] Pavy 'On Diabetes,' 2nd ed. p. 166.

together the results of many post-mortems, we find every degree of congestion and many varieties of hyperæmic and inflammatory change. Within the tubes over-growth and fatty impregnation of the epithelium abound.

The gland is often soft from fatty degeneration. Its occasional hardness would seem to imply some such increase of the fibrous tissue as is produced by cardiac congestion, but this occurs more rarely or more rarely leads to granulation and shrinking when of diabetic than when of valvular origin.

Probably fibrosis is more apt to result from passive or mechanical congestion, such as heart disease produces, than from the active though not necessarily acute hyperæmia of diabetes dependent upon exaltation of function. In the latter case the influence chiefly tells upon the epithelial and working glandular elements causing fatty change and tubal accumulation.

Whether from this cause or some other the fibroid changes which lead to granulation and contraction are apparently not more common in persons who have diabetes than in those who have not.

Prout[1] noticed in connection with diabetes 'an enlarged, flaccid, and occasionally a congested state of the kidneys; a section of which organ, when first removed from the recently dead body, has frequently assumed on exposure to the air a peculiar deep orange-red tint difficult to be described.'

The annexed table shows the condition of the kidneys in the cases of the disease examined at St. George's Hospital since the commencement of the records.

[1] 'On Stomach and Renal Diseases,' 4th ed. p. 39.

State of the Kidneys in 27 Diabetic Subjects examined at St. George's Hospital between the years 1842 and 1873.

Kidneys natural in		2
Congestion 12	Congested, in some cases swollen	6
	Coarse, or coarse and congested	5
	Containing ecchymoses	1
Tubal 7	Fatty and congested	1
	Fatty and enlarged	2
	Large, pale, smooth, mottled	4
Intertubal 5	Slightly granular	1
	Granulated and contracted	2
	Contracted, or granular, and cysted	2
One containing cheesy mass surrounded by fibrous capsule		1
Total number of post-mortems		27

The preponderance of congestive and sub-inflammatory changes is striking. The albuminuria of long-standing diabetes gives evidence during life of the morbid stimulation which the disease brings to bear upon the kidney.

OTHER ORGANS.

It is not necessary to describe in detail the condition of the other organs after death by diabetes. It is enough to state that a general wasting prevails. This is evident in the heart, which, as in phthisis, is often found to be considerably below its natural size. In a man who died at St. George's Hospital of the disease in question, the heart, not altered but in bulk, weighed only 6½ ounces. In another it weighed but 4½. The muscular substance of the ventricles is often yellow, soft, and fatty. There is in this disease no especial tendency to atheroma or endocarditis. The larger vessels as well as the least are usually smooth and natural to the naked eye, unlike what is found with albuminuria ; and from the absence of hypertrophy of the heart it may be inferred the microscopic changes in the minute vessels are also wanting.

The voluntary muscles have been noticed as florid and dry as after death by cholera, but I am not able to assert that this condition is generally apparent.

Blood.

Perhaps no more convenient place than the present can be found for stating what is known of the blood in diabetes, though since it has always been drawn during life, the description might with as much propriety be placed in the clinical division of the subject.

The chemistry of the blood in this disorder as in others needs reconstruction; the results obtained by the old methods may be shortly stated. Simon,[1] whose observations upon diabetic blood, though of old date, have not, so far as I know, been materially added to or contradicted, gives the following results of its analysis in three cases. I have annexed for comparison an analysis of healthy blood by the same chemist.

In 1,000 parts.	In Health.	Diabetes.		
		Case 1.	Case 2.	Case 3.
Water	791·900	794·663	789·480	802·000
Solid constituents	208·100	205·337	210·510	198·000
Fibrin	2·011	2·432	2·370	2·030
Fat	1·978	2·010	3·640	2·250
Albumen	75·590	114·570	86·000	97·450
Globulin	105·165	66·300	98·500	74·350
Hæmatin	7·181	5·425	5·100	37 000
Sugar	——	2·500	trace	trace
Extractive matters and salts.	14·174	9·070	14·900	12·680

The following analyses by other chemists are cited by the same writer; to which for comparison, I have adjoined the mean results of 10 analyses of healthy venous blood by Lecanu.

[1] Simon's 'Animal Chemistry,' Sydenham Society's edition, vol. i. p. 327.

In 1,000 parts.	In Health. Means of 10 Analyses.	Diabetic Blood.		
		Bouchardat.	Henry and Souberan.	Lecanu.
Water	789·320	808·76	816·50	848·35
Solid constituents . .	210·680	191·24	183·50	151·65
Fibrin	——	1·95	2·43	——
Albumen	68·059	62·54	55·48	58·47
Blood corpuscles . .	132·490	118·25	120·37	85·18
Salts	——	8·52	5·57	8·00
Extractive matter, salts, and colouring matter	10·688			

From these and other analyses it would seem that, saving the introduction of sugar and the increase of fat, the changes which the blood undergoes are chiefly, as would be expected, in the direction of impoverishment.

The water is increased and the total solids diminished, the diminution relating most markedly to the corpuscles. The albumen, according to most observers, is lessened, though it did not appear so in Simon's cases. In this particular much must depend upon the time relatively to food at which the blood is abstracted. The salts where changed appear to be lessened; the fibrin not much altered.

The only normal constituent of the blood, unless sugar be so regarded, which undergoes marked increase is the fat.

Excess of oil in blood.

Other observers have found this increase to a larger extent than Simon. In one analysis the fat amounted to 6·77 in 1,000 parts of diabetic blood. This seems at first sight inconsistent with the deficiency of fat in the tissues. The tissues, however, probably obtain their fat not only from what is introduced as such but from some of the substances which in this disease are expelled as sugar. The excess of fat in the blood may be associated with the large consumption of animal food usual in the disease, and the fact that its fatty part, unlike its protein portion, appears to elude saccharine metamorphosis.

The leading peculiarity of diabetic blood is the presence

of sugar. This is found most abundantly two or three hours after dinner. With fasting the sugar becomes inappreciable. Owen Rees found 1·8 parts of sugar in 1,000 parts of the serum of diabetic blood; a result which is not very remote from the proportion stated by Simon. Sugar does not abound only in the blood, but appears to permeate the whole body.

Glycosuria in Insanity.

Having regard to the resemblance which the diabetic nervous changes bear to those of some forms of so-called mental disease, more particularly of general paralysis, it is of interest to enquire how far glycosuria is a concomitant of insanity. To ascertain this point I had recourse to Bethlem Hospital, and here beg to acknowledge the liberality with which the opportunities for observation afforded by that great establishment were placed at my disposal by Dr. Williams, as well as the personal assistance I received from Dr. Savage and Mr. Williams, at that time his clinical assistant. With the help of these gentlemen I examined the urine of 106 lunatics, testing for sugar with Fehling's solution and also with liquor potassæ, and for albumen in the ordinary way.

If the urine destroyed the colour of half its bulk of Fehling's solution, representing, supposing the discharge of colour to be wholly due to sugar, a proportion of ·12 per cent., it was described as giving a trace of reduction. If it decolorised its own bulk of the test solution, implying ·25 per cent. of sugar, it was described as giving decided reduction. If a bulk of solution exceeding that of the urine was similarly affected, it was registered as considerable reduction.

Examination of the Urine especially with regard to the presence of Sugar in 106 Insane Persons, Inmates of Bethlem Hospital.

	Number tested	Fehling's solution				Liquor Potassæ, darkened by boiling with	Albumen
		No reduction	Trace of reduction	Decided reduction	Considerable reduction		
Mental Weakness . .	12	10	2			1	
Chronic dementia . .	3	2	1				
Acute ,, . .	2	1	1				
Melancholia . . .	31	15	9	7		5	1
,, puerperal .	2	1	1				
Convalescent from Melancholia . . .	2	1	1				
Melancholia and hypochondriasis . .	1			1			
Chronic mania . .	21	13	5	3		4	2
Recurrent mania . .	4	3	1				
,, ,, puerperal	1		1				
Acute mania . . .	15	6	5	3	1	2	1
,, ,, syphilitic .	1				1	1	
Convalescent from acute mania . . .	3	1	2				
General paralysis . .	6	4		1	1	1	
Uncertain . . .	2	2					
Totals	106	59	29	15	3	14	4

The results are as follows:—

Of the 106 specimens examined, 47 reduced copper in one or other degree; 29 to the smallest extent noticed; 18 more largely, in 3 of which the reaction was such as to indicate a considerable amount of sugar. It is quite possible that the reduction of copper when only in the lowest degree, may, in a few instances, have been due to some peculiarity in the urine other than saccharinity; but with the larger degrees of reduction which were found in one-sixth of the cases, this source of error could scarcely have intervened. It will be noted that in no less than 14 cases, the amount of sugar was large enough to be recognised by the comparatively rough test, boiling with liquor potassæ.

In no instance was the sugar so abundant as to give obvious diabetic characters to the urine or to the symptoms.

Evidences of sugar were found with the greatest frequency in mania, particularly in the acute shape, and

melancholia. In acute mania and in melancholia a trace of sugar is the rule rather than the exception.

The infrequency of albumen in these cases as compared with the inmates of ordinary hospitals is as striking as the frequency of traces of sugar.

As a corollary to these statements, I may mention that a very distinct amount of sugar is often to be detected in the urine of children with tubercular meningitis, though I am not prepared to state the proportions numerically.

CHAPTER III.

SUBJECTS, DISTRIBUTION, AND CAUSES OF DIABETES.

SUBJECTS.

DIABETES attacks men more often than women. Sex.

Of 29 persons who died of it at St. George's Hospital, 23 were males, 6 females.

From the Registrar-General's Reports we learn that in England and Wales for the ten years ending with 1870, 4,271 males, 2,223 females, died of this disease.

Diabetes affects the middle of life rather than the extremities. It is unknown in infancy, rare, though rapidly fatal, in childhood; towards maturity it becomes more frequent, and is common between 30 and 60. With advancing years it occurs less often until with extreme age it is almost as infrequent as at the outset of life. Age.

The annexed table shows the age at which 29 fatal cases terminated.

Of 29 *Persons who died of Diabetes at St. George's Hospital the youngest died at the age of* 6, *the oldest at* 73.

					Persons.
Between the ages of		5 and	9	there died	1
,,	,,	10	19	,,	3
,,	,,	20	29	,,	6
,,	,,	30	39	,,	10
,,	,,	40	49	,,	6
,,	,,	50	59	,,	2
,,	,,	60	69	,,	0
,,	,,	70	79	,,	1
					29

As furnishing information, which, though less accu-

rate, is more extensive, I have subjoined a table compiled from the Registrar-General's Reports for England and Wales for the ten years ending with 1870. It is necessary to observe that the cases described as diabetes at the earliest periods of life were probably of the insipid variety for which there is no separate entry in the Registrar's table.

Sex and Age of the Subjects of Fatal Diabetes in England and Wales for the ten years 1861–1870.

	Males.	Females.	Total.	Proportion of Deaths from Diabetes to number of persons alive of the stated age. = 1 in
Under 1 year . . .	4	4	8	
1 year old . . .	10	9	19	
2 years ,, . . .	12	4	16	
3 ,, ,, . . .	7	8	15	
4 ,, ,, . . .	8	8	16	
Total under 5 years .	41	33	74	378,253
5 to 10 years . .	62	52	114	205,649
10 ,, 15 ,, . .	113	87	200	10,525
15 ,, 20 ,, . .	221	131	352	5,490
20 ,, 25 ,, . .	222	141	363	5,039
25 ,, 35 ,, . .	651	368	1,019	2,900
35 ,, 45 ,, . .	653	384	1,037	2,274
45 ,, 55 ,, . .	746	352	1,098	1,582
55 ,, 65 ,, . .	817	377	1,194	980
65 ,, 75 ,, . .	594	236	830	792
75 ,, 85 ,, . .	146	55	201	1,195
85 ,, 95 ,, . .	7	7	14	2,296
95 ,, ,, and upwards .	—	—	—	—
Total of all ages .	4,271	2,223	6,494	

The absolute numbers show that death from diabetes frequently occurs during the half-century of life from 25 to 75. From 25 to 65 the mortality is pretty evenly spread, afterwards it appears to diminish. Comparing, however, the mortality from diabetes with the number of people alive at each period of life—a number which necessarily lessens with each advance in age—it is seen that a larger proportion of persons between 65 and 75 fall victims to diabetes than at any other epoch.

Men on an average die of diabetes somewhat later

than women. Male deaths from this cause are most numerous between 55 and 65, while with women such deaths become more numerous up to the age of 45, and then cease to increase.

Diabetes mellitus, as I have said, is all but unknown in infancy, though diabetes insipidus is common. The earliest case of true diabetes which I have seen, proved fatal after six months' illness, at the age of 6. Dr. Bence Jones tells us that the age of the youngest diabetic patient he knew was 3½ years. Dr. Roberts[1] mentions as the earliest instance within his experience a boy who was diabetic at the age of 3. A still younger victim to the disease, as far as I know, the youngest on record, is mentioned by Dr. James L. Brown.[2] The case is so exceptional in the tender years of the patient that one might think some error had crept in, were it not related with circumstance and verisimilitude.

Instances of diabetes in childhood—its rarity.

A little girl became diabetic at the age of 20 months and died before completing her second year. She passed five pints a day of urine which was saccharine but not albuminous, and ranged in specific gravity from 1,030 to 1,036. The vulva became erythematous; the breath acquired an odour like that of chloroform; she became emaciated and, after occasional febrile attacks, sank from exhaustion.

The post-mortem showed general miliary tuberculosis. The brain in particular was injected and the arachnoid thickened, while miliary tubercles were found in the Sylvian fissures, and by hundreds on the choroid plexuses.[3]

Probably the nature of this case would have been more truly expressed if it had been called one of glycosuria dependent on tubercular disease of brain. Slight glycosuria from this cause is not uncommon however young the child.

[1] 'Roberts On Urinary and Renal Diseases,' 2nd ed. p. 216.

[2] 'Lectures on Pathology and Therapeutics,' p. 55.

[3] 'American Journal of Obstetrics,' 1868. Quoted in the 'Half-Yearly Abstract,' Jan. to June, 1869, p. 348.

Thus diabetes belongs chiefly to the time of maturity; and we are led to ask whether, as has been thought, it is connected in its origin with the reproductive function, or, as seems more probable, with the use and wear of the brain. To answer this question we have but to see how far the tendency to diabetes is determined by the periods, sufficiently widely separate, of sexual and mental activity.

Belongs to mature life; related not to sexual but cerebral functions.

Diabetes, in the male at least, numbers its victims increasingly up to an age at which the diseases of youth have long been replaced by the degenerations of age. Though rare before puberty it continually occurs after the sexual functions have subsided into the dormancy of age. It keeps pace, not with the vices of youth, but with the acquirement of advancing years, 'the written troubles of the brain,' which each year inscribes more deeply until time causes the point to fade.

With women the frequency of the disease shows no marked increase after the period of child-bearing, a time at which many of the anxieties which beset the female come to an end.

The diabetic epoch is not very different, though somewhat later, than that of insanity.

It is worth a passing remark, though not strictly in place, that the severity of diabetes varies inversely with the age of the patient. Most acute and surely fatal in early life; chronic, often intermittent, and least injurious in old age.

Temperament.

Prout noticed the disease more often among persons of 'sanguine temperament with light or reddish hair,' than with others; and it is easy to recall many instances in which it has occurred with a light freckled complexion and sandy hair. But though individuals of the Saxon type are frequent victims, no tint of skin or hair confers exemption, and it must be left in doubt whether persons presenting these characteristics are attacked with more frequency than would occur were the disorder impartially distributed, taking into consideration the large proportion which they form of the population of England.

Geographical Distribution of Diabetes in relation to its Etiology.

We may look to the geographical distribution of diabetes for some light upon the causes from which it springs. Diabetes is a disease so strictly defined and so easily capable of exact diagnosis, that unless our costly and elaborate system of registration be absolutely worthless, we may appeal to it on this matter for trustworthy information.

In this hope I have ascertained how often death has been attributed to this disease in all the counties of Great Britain for the space of ten years. Where such deaths are few, as in all but the larger counties, no shorter period would give a valid result. The annexed columns show, for each county, the absolute number of deaths from diabetes; the proportion which such deaths bear to the population as ascertained at the end of the decennial period; and the proportion which they bear to the aggregate of mortality.

Deaths from Diabetes in Counties of England and Wales for ten years, 1861–1870.

Total number of deaths from diabetes in each county in adjoining column	Compared to population according to Census of 1871 and arranged accordingly		Compared to total deaths from all causes in the ten years and arranged accordingly	
	One death in 10 years to population of :—		One death in 10 years to mortality of :—	
212	Norfolk	2,030	Berkshire	394
108	Berkshire	2,095	Norfolk	425
26	Huntingdon	2,232	Suffolk	431
155	Suffolk	2,237	Huntingdon	453
93	North Riding	2,524	Westmoreland	470
104	Leicestershire	2,644	Sussex	487
122	Derbyshire	2,663	North Riding	490
133	Nottinghamshire	2,671	Dorsetshire	540
24	Westmoreland	2,713	Derbyshire	546
60	Oxfordshire	2,735	Leicestershire	547
151	Sussex	2,787	Nottingham	552
91	Shropshire	2,823	Worcester	566
107	East Riding	2,857	Wiltshire	573
65	Cambridgeshire	2,953	Oxfordshire	577
64	Dorset	2,953	Cambridgeshire	580
52	Buckingham	2,980	Shropshire	586

Deaths from Diabetes—continued.

Total number of deaths from diabetes in each county in adjoining column	Compared to population according to Census of 1871 and arranged accordingly		Compared to total deaths from all causes in the ten years and arranged accordingly	
	One death in 10 years to population of:—		One death in 10 years to mortality of:—	
112	Worcestershire . .	3,001	Buckinghamshire .	589
81	Wiltshire . . .	3,020	Lincolnshire . .	597
128	Northumberland .	3,023	Hertfordshire . .	609
583	West Riding . .	3,180	East Riding . .	612
133	Lincolnshire . .	3,219	Rutlandshire . .	634
161	Cheshire . . .	3,316	Essex	660
7	Rutlandshire . .	3,340	Northumberland . .	660
58	Hertfordshire . .	3,355	Extra-metropolitan parts of three metropolitan counties, as one	663
184	Warwickshire . .	3,425	(Extra-metropolitan part of Surrey) . . .	651
141	Gloucestershire . .	3,464	(Extra-metropolitan part of Kent)	667
248	Staffordshire . .	3,537	(Extra-metropolitan part of Middlesex) . .	668
42	Bedfordshire . .	3,608	Gloucester . . .	695
61	Cumberland . .	3,610	Cheshire . . .	700
785	Lancashire . .	3,623	West Riding . .	717
121	Essex . . .	3,643	Bedfordshire . .	719
859	London . . .	3,793	Warwickshire . .	730
65	Northampton . .	3,816	Somerset . . .	771
327	Extra-metropolitan parts of three metropolitan counties, as one . .	3,848	Northamptonshire .	773
86	(Extra-metropolitan part of Surrey) . .	4,245	Staffordshire . .	775
173	(Extra-metropolitan part of Kent) . . .	3,574	Cumberland . .	777
68	(Extra-metropolitan part of Middlesex) .	3,895	Herefordshire . .	851
120	Somerset . . .	4,021	London . . .	857
87	Cornwall . . .	4,116	Cornwall . . .	871
51	Monmouth . .	4,305	Hampshire . . .	874
25	Herefordshire . .	4,346	Monmouth . . .	888
110	Hampshire . .	4,776	Lancashire. . .	915
123	Devonshire . .	4,922	Devonshire . . .	984
137	Durham . . .	5,414	Durham . .	1,074
78	North Wales . .	5,651	North Wales .	1,180
92	South Wales . .	8,460	South Wales .	1,706

Deaths from Diabetes in Counties of Scotland for ten years 1861–1870.

Total number of deaths from diabetes in each county in adjoining column	Compared to population according to Census of 1871 and arranged accordingly		Compared to total deaths from all causes in the ten years and arranged accordingly	
	One death in ten years to population of:—		One death in ten years to mortality of:—	
5	Kinross	1,583	Kinross	281
15	Wigtown	2,573	Kincardine	473
15	Linlithgow	2,758	Berwick	488
12	Kincardine	2,924	Peebles	496
29	Dumfries	2,925	Wigtown	500
12	Berwick	3,031	Dumfries	524
4	Peebles	3,054	Banff	527
12	Haddington	3,146	Selkirk	548
18	Banff	3,271	Haddington	582
74	Aberdeen	3,328	Aberdeen	584
16	Roxburgh	3,347	Linlithgow	589
93	Edinburgh	3,528	Roxburgh	625
4	Selkirk	3,583	Caithness	671
56	Ayr	3,587	Fife	717
17	Dumbarton	3,595	Sutherland	719
25	Stirling	3,733	Elgin	723
42	Fife	3,831	Dumbarton	738
33	Perth	3,895	Edinburgh	772
11	Elgin	4,049	Ayr	774
10	Caithness	4,101	Stirling	778
4	Bute	4,283	Perth	788
176	Lanark	4,471	Orkney	805
5	Sutherland	4,659	Inverness	870
50	Forfar	4,800	Bute	928
17	Inverness	4,956	Forfar	1,056
6	Orkney	5,212	Lanark	1,108
4	Clackmannan	5,557	Clackmannan	1,126
12	Argyll	6,638	Argyll	1,216
28	Renfrew	6,975	Ross and Cromarty	1,358
10	Ross and Cromarty	8,209	Shetland	1,613
1	Nairn	8,372	Nairn	1,670
3	Shetland	10,539	Renfrew	1,706
2	Kirkcudbright	21,043	Kirkcudbright	3,886

To guard against error by looking from different points of view, it is necessary to take the frequency of the disease in question both in relation to the population of each place and also in relation to its death rate from all causes. Each point of view may comprise certain fallacies, but since the fallacies of each are different, where they agree we may accept the common indication.

The following conclusions are sufficiently obvious. Diabetes is more abundant in agricultural districts than where the inhabitants are engaged in manufactures and

mining. It is more common in the colder than in the warmer counties. It is not especially frequent where ague abounds, as has been sometimes thought, nor can we trace it, as has been also supposed, to cider, since in the counties where this beverage is produced, it is, as compared with the rest of England, almost at its minimum.

More frequent in agricultural than in manufacturing counties.

The conclusion that the disease is more common among tillers of the soil than among manufacturers and miners similarly situated, is evident from whatever point of view the figures be regarded.[1] Norfolk and Suffolk, Berkshire and Huntingdon, where cold and agriculture co-operate, suffer the most severely. By one standard of comparison, the 19 counties most affected, by the other the 28 most affected, are chiefly devoted to husbandry. The great industrial centres, the West Riding with its manufacturing population, Warwickshire, including Birmingham and Coventry, Lanark including Glasgow, Staffordshire, with its potteries and coal-mines, Lancashire and London, all display the disease in diminished frequency. And comparing adjoining but differently employed districts, we find a larger proportion of diabetes in the North and East Ridings of Yorkshire, which are chiefly agricultural, than in the manufacturing West. In North Wales, almost wholly bucolic, we find more of it than in South Wales, where coal and iron abound.[2] Thus if we take agriculture, as we generally may, to represent want and exposure, we may say that those conditions predispose to diabetes.

The greater prevalence of the disease in the colder than in the warmer agricultural counties is sufficiently evident on comparing Cornwall, Devonshire, Hampshire,

[1] Dr. Roberts, whose views always command respect, has advanced the contrary conclusion, believing that 'urban and manufacturing districts suffer more from diabetes than rural districts.' He however appears to have based his view upon the examination of one year's report only, and upon a less minute subdivision of the kingdom than the annexed tables afford. ('On Urinary and Renal Diseases,' 2nd ed. p. 217.)

[2] We may fairly compare North with South Wales, though it is probable that the greater imperfection of Welsh registration would introduce error into a comparison between Wales and England.

and Somerset with counties similarly employed but differently situated, such for example as Norfolk and Suffolk on the east coast, or the bleak North and East Ridings. Cold.

The table for Scotland represents a greater variety of climate than that for England, and gives a greater variation in the prevalence of diabetes. In the more remote districts it is probable that the registration is not accurate enough to allow of very trustworthy comparison. The eastern counties, which are more exposed to cold than the western, are more diabetic, Wigtown among the western being a notable exception. The influence of occupation is less marked than that of climate.

CAUSES OF DIABETES.

Of the many causes which have been assigned for diabetes, some appear to be altogether imaginary, while others are not so much causes of the disease as consequences of its earliest stage. Others again, like the abundant use of saccharine food, must probably be regarded rather as causes of temporary glycosuria than strictly of diabetes.

Diabetes is often hereditary. It can sometimes be traced to perturbation of mind and sometimes to mechanical injury of the nervous centres. These are, I will not say, the only possible causes, but those only of which we can be absolutely sure. More often than not the disease arises as if it were part of the necessary career of the individual without any circumstance which we can isolate as its progenitor.

With this compendium of the etiology of the disease, I will consider in detail some of the causes to which it has been ascribed.

Hereditary influence.

Of the circumstances which determine the occurrence of diabetes, hereditary influence is one of the most frequently evident. Whether regarded as exciting or predisposing, it is certain that this cause is efficient without

the traceable intervention of any other. All writers on diabetes recognise, and most practitioners must have witnessed, its tendency to run in families.

Sir Henry Marsh[1] refers to an instance, not, however, as under his own observation, in which the disease was transmitted from parent to child, like a biblical curse, unto the fourth generation.

It frequently happens that the disorder breaks out in two consecutive generations, both as affecting parents and children, and also as passing to the nephew or niece of the person originally attacked. Dr. Pavy mentions a case in which both the father and the aunt of a diabetic man had died of the disease; another in which two daughters which were born to a diabetic father by different mothers (one begotten before, the other after, he became subject to the disease), both became diabetic. A boy was under my care for diabetes, of which he died at the age of 18. Three years after his death his father presented himself, having been recently attacked with the same disease.

It is also common for several members of a family belonging to the same generation to suffer. Dr. Roberts mentions a family of eight children all of whom became diabetic though the parents were healthy. Dr. Pavy refers to a family of seven of which four members, two brothers and two sisters, became subjects of the disease; to another in which three brothers were affected. Sir Thomas Watson had under his observation three children, two brothers and their sister, all affected with diabetes.

Two sisters, one of whom was a patient of mine, simultaneously suffered from the disease in question, at the ages respectively of 24 and 16. Indeed the sharing of the disease by two brothers, or by a brother and sister, is a familiar experience.

But easy as it is to collect and recall instances of consanguinity among diabetic subjects, and sufficient as they are to prove the existence of hereditary influence as one of the causes of the disease, yet these instances are but

[1] 'Dublin Quarterly Journal,' vol. xvii., New Series, p. 17.

few as compared with cases in which no family proclivity can be traced. 29 examples of fatal diabetes at St. George's Hospital gave only two in which any hereditary influence or family tendency could be traced. Of 225 cases collected by Griesinger the disease was traced in the family only in three.

Mental emotion.

Of all the causes of diabetes mental emotion is the one which we can most often trace and which we must believe to be the most frequent. We may say of this disorder with more truth than of that to which the words were applied: 'It hath its original from much grief; from study and perturbation of the brain.'

From the time of Thomas Willis, who traced the disease to 'sadness or long sorrow,' there have been few writers who have not recognised its mental origin. Prout attributes it, among other causes, to mental anxiety or distress, and suggests that the supposed immunity of the lower animals from glycosuria (an immunity which later observations have shown not to be in all circumstances invariable) may be referred 'to the absence of that fertile cause of bodily disorder in human beings, the influence of mind.'

It is scarcely necessary to adduce examples of so common a sequence as that of diabetes upon mental disturbances. Grief, anxiety, protracted intellectual toil, violent anger and mental shock, might all be shown to be directly productive of this disease.

In the experience of Rayer the disease came on after a violent fit of passion. Dr. Roberts tells us that in one of his patients the disease 'followed on distress of mind caused by an unjust suspicion of theft; in another it followed the burning down of his place of business; in a third it was attributed to anxiety attendant on a Chancery suit.'

A young woman died in St. George's Hospital, seven months after the death of her husband, of diabetes apparently brought on by inordinate grief.

A child fell from a third-floor window and was smashed

upon the pavement to all appearance hopelessly. But the accident was more fatal to its mother than itself. The child survived. The mother, who was abruptly made aware of the accident, never recovered the shock. For three weeks she, to use her own words, could neither eat nor sleep. Within two months she became much emaciated, was consumed with thirst, and was passing water in great quantities which incrusted upon and stiffened any garment it touched. She died of diabetes within ten months of the occurrence upon which it had succeeded.[1]

Dr. Garrod relates the following remarkable instance of diabetes produced by brief but probably somewhat severe apprehension. 'Two gentlemen fought a duel in Holland: after the first had fired he remained for some time in a state of suspense, from his adversary's pistol once or twice missing fire. He was uninjured, but, a day or so after, became diabetic.

A young military officer now under my care sat up while at a foreign station with a sick and delirious comrade for six weeks with little intermission. He suffered much himself from anxiety and want of sleep, but he apparently recovered his health and retained it until three months afterwards, when an excoriation on the penis with profuse urination led to the discovery of diabetes, which had set in in a severe form.

It sometimes happens that the disease will come on with apparent severity during the pressure of toil or anxiety and will subside on its conclusion.

For the following case in which diabetes arose on two separate occasions under the influence of anxiety I am indebted to Dr. Hermann Weber.

A. C., a merchant 47 years of age, whose father had died of diabetes at the age of 64, consulted Dr. Weber in July 1857 in consequence of having passed uric acid in concretions which varied from the smallest size up to that of a large hemp-seed. The urine examined on various

[1] See case of Mackay, related subsequently.

occasions was of medium specific gravity (1,016 to 1,022), it freely deposited lithic acid crystals, and contained neither albumen nor sugar. He was sent to Carlsbad and came back in good health, the urine being less acid, and, as before, free from albumen and sugar.

During the November and December of the same year he was under constant excessive anxiety, fearing that his business was ruined, and that the property of his own family and that of many others would be sacrificed. After many sleepless nights he became delirious or rather insane—for there was no pyrexia—and almost suddenly began to pass urine very frequently and in large quantities. It was found to contain abundance of sugar. The daily quantity of urine varied from 7 to 9 pints; and the specific gravity from 1,036 to 1,044.

Under the influence of medium doses of opium (only to procure sleep), and regulated diet, he became more quiet and the quantity of urine decreased; but the assurance that his business had passed safely through the crisis seemed to do more to give him sleep than the medicine. Within three weeks the urine was free from sugar, and so remained, as ascertained by several annual examinations, until the year 1866.

During the mercantile crisis of that year A. C. again became restless, sleepless, and diabetic. After the crisis he again recovered completely and remained well, with perhaps a single exception, up to 1870.

At the outbreak of the Franco-Prussian war in this year he became much excited and died of apoplexy.

Dr. Pavy relates the case of a gentleman who became diabetic under the influence of mental excitement, and ceased to be so when retirement from town and professional duties had enabled his mind to recover its equipoise.

Sexual excess, especially in the male, or the combination of evil influences comprised under the term dissipation, must be mentioned among the more infrequent causes of diabetes. A patient of mine who died at the age of 25, in whom the disease took so severe a form that as much Sexual excess.

as 50 ounces of sugar (more than three pounds) were secreted in twenty-four hours—the largest production I have ever witnessed in diabetes—appeared to have owed his disease to this cause. From the age of 17 he had been addicted to promiscuous sexual indulgence, and so extravagantly, that in the absence of any other cause for the disease I was fain to ascribe it to this. But there is no evidence that this vice is other than a rare source of diabetes. Sexual excess or abuse is more apt to engender especially spinal lesions, such as are declared by paraplegia and ataxy, than one which, like diabetes, is essentially cerebral.

Alcohol.

Willis attributed the disorder[1] to the daily and immoderate drinking of cider, ale, and acid wines, and many subsequent writers have hypothetically ascribed it to alcohol. I cannot, however, find that the complaint is more frequent with drunkenness than sobriety, though analogy would lead us to expect that the hyperæmic and degenerative changes of brain which constitute the disease would be invited by this agent so especially destructive to cerebral tissue. It has never happened to me in enquiring into the antecedents of diabetes to be able to associate its origin with drink; and the same absence of clinical evidence of this kind is to be remarked in the recorded experience of those who have seen most of the disease. Griesinger in his compilation of 295 cases finds a history of decided drunkenness in 9, probably not more than an inevitable proportion.

Of the series of traders in liquor, 149 in number, whose diseases, as illustrating the effects of alcohol, formed the subject of a paper I read before the Medico-Chirurgical Society,[2] not one was diabetic. If diabetes be an effect of alcohol, it is the only effect of which this series gave no example. Prout indeed, with Willis, attributed diabetes to the drinking of cider, but this view is not supported by the registration of the cider counties,

[1] 'On the Operations of Medicines in Man's Body,' p. 74.

[2] 'Medico-Chirurgical Transactions,' vol. lvi.

both Devon and Hereford presenting a less than average mortality from this cause (see p. 70). Apart from the influence of alcohol, several observers, including both Prout[1] and Trousseau,[2] have assigned diabetes to the immoderate drinking of cold fluids while heated; it is, however, a possible explanation of such cases that the disease was present before though unobserved, and was the cause rather than the consequence of the 'devouring thirst' thus quenched.

Starchy or saccharine food.

Diabetes has been thought to arise from saccharine or starchy food. There is no doubt that when sugar is taken in excess, some will escape with the urine; but whether true diabetes ever results from this cause is more than doubtful. Griesinger mentions a man who was attacked with the disease after working for two years in a sugar factory, but adds that of 12 others identically employed none suffered. Three other examples, two of them fatal, have been collected by the same author, in which the disease has appeared in sugar refiners; but the infrequency of such cases, notwithstanding that their attractive simplicity would ensure their notice and record, is enough to make one doubt whether sugar operatives have more than their share of the disease. Negroes on sugar plantations, who grow fat upon the cane, are known not to be especially liable to diabetes.

Griesinger quotes the instance of a child who became diabetic, as was supposed, from a diet of water gruel; but if starchy food is capable of causing this result, how many of the children of the poor would escape?

Other diseases as antecedent to diabetes.

The disorder has been sometimes thought to manifest itself as a sequel to some other complaint. The industrious compiler already quoted, out of his 225 cases, assigns 3 to continued fever; 1 to scarlet fever; 1 to pleurisy; 1 to acute rheumatism; and 10 to intermittent fever.

The last is the only disorder which need occupy our

[1] Prout, loc. cit. p. 36.

[2] Trousseau's 'Clinical Lectures,' vol. iii. p. 492.

attention as with any possible frequency instigating diabetes. Prout, whose observation was seldom at fault, thought that the predisposition to diabetes was sometimes acquired by residence in a malarious district. Registration, however, does not show any marked prevalence of the disease in the counties of England where ague is most common. Cambridgeshire and Lincolnshire, indeed, stand above the middle of the list, but there are no less than 13 counties, all agricultural, in which the disease on every showing is more prevalent than in either. Probably Cambridgeshire and Lincolnshire do not display more diabetes than is due to cold and agriculture.

Malaria.

Cold.

Diabetes has been attributed to cold and wet; and the geographical distribution of the disease shows that this belief is not without foundation, though the disorder can be traced to other causes with more directness and certainty than to this. Diabetes is more common in the colder than in the warmer counties, and where agricultural pursuits involve exposure to weather, than where manufactories and mines give cover (see p. 68).

External cold, and the drinking of cold fluids while heated, are among the causes of the disease enumerated by Prout; and Griesinger refers 26·3 per cent. of his collected cases to accidental or habitual exposure.

It is probable, however, that in many of the cases which went to make this large percentage the disorder was assigned to cold or wet chiefly because no other cause could be found. Cold, like alcohol, is always at hand to fill an etiological vacancy. In some of the instances in which the complaint has immediately followed upon cold, as in one recorded by Sir Henry Marsh,[1] other causes have been conjoined. A man after peril by sea became diabetic; he had been exposed to wet and cold, also to privation and anxiety.

Whatever influence cold may have in causing, or predisposing to, diabetes, it is certain that in both regards it

[1] 'Dublin Hospital Reports,' vol. iii. p. 441.

is immeasurably less effective than other circumstances. Dr. Pavy states that cold as a cause of diabetes has not come within his experience, and my own opportunities have given the same negative result.

Injuries and obvious Morbid Lesions of the Brain in connection with Diabetes.

Since the cardinal discovery of Bernard, pathologists have been on the watch for instances in the human subject associating glycosuria with injury of the brain wrought by violence or disease. Numerous, or I may perhaps say innumerable, examples have rewarded their search. These may be for practical purposes divided into two classes:—the first comprising cases in which some mechanical hurt or easily recognisable morbid change has been followed by temporary saccharinity of urine which subsides, should the patient survive, with or before the other results of the lesion;—the second including those in which one of these causes has set up glycosuria, which proves permanent, or at least persists long after the other effects have subsided, and does not differ either in its attendant symptoms or its final issue from diabetes otherwise engendered.

Cases in point have been recorded by many recent writers, Bernard himself setting the example; while one at least has been unearthed from a clinical record of the pre-Bernardian epoch—one left by Baron Larrey, the surgeon of the first empire, whose observation, read by the light of other days, has a bearing almost prophetic.

M. Fischer,[1] who deserves the gratitude of everyone interested in traumatic diabetes, has written a paper which may be appealed to as a compendium of experience

[1] 'Archives Générales de Médicine,' 1862, pp. 257, 413. A valuable paper on the same subject was also published by M. Fritz, in the 'Gazette Hebdomadaire' for the year 1859 (vol. vi.). The cases here given, however, which are numerous, are for the most part reproduced along with others in M. Fischer's paper, so that the latter may be appealed to as comprising the facts of the former.

on this question up to the year 1862, and in what is to follow I shall make liberal use of the cases he has collected.

He gives 43 instances of the traumatic origin of glycosuria or polyuria ; 21 in which one of these affections has succeeded upon injury of the head ; 22 in which one of them has ensued upon accidents involving other parts of the body.

Polyuria or mere superabundance of urine will be considered elsewhere, and may here be dismissed with the observation that it was noted in four of the 21 cases of cranial lesion.

Limiting our view at present to glycosuria as resulting from injuries of the head, of M. Fischer's 17 examples :—

Polyuria with slight glycosuria was found in . .	3	cases
Transient glycosuria was found in	6	,,
Permanent glycosuria, or confirmed diabetes, was found in	8	,,
	17	

Five of these glycosuric cases were of ascertained fracture of the skull which in most cases involved the base. Twelve were of wounds and contusions without recognised fracture.

With regard to the place of the blow this was :—

In front in	3	instances
On the vertex, or sides, in	4	,,
On the occiput in	5	,,
Undetermined in	5	,,
	17	

No longer limiting myself to M. Fischer, though freely using his valuable collection of cases, I will bring together a few examples which may sufficiently, and not too lengthily, illustrate the origin of diabetes in hurts of the brain by violence or coarse disease.

First with regard to slight or transient glycosuria; and beginning with the cases where the change of urine was least, it will be seen that slight saccharinity with much increase of this secretion is no infrequent result of severe injuries of the head.

Slight glycosuria of traumatic origin.

A zinc-worker,[1] 17 years of age, fell from a building upon which he was at work and received a complicated fracture of the skull with much injury of the face, for which he was admitted into the Lariboisière Hospital under the care of M. Chassaignac. He had some epileptiform attacks followed by temporary loss of consciousness. Much suppuration occurred about the face in connection with injury of the right orbit. Five days after the accident he became very thirsty and passed an increased quantity of urine which was found to be clear and limpid and to contain sugar in the proportion of 3·25 per 1,000. The patient became delirious, then comatose, and died thirteen days after the fall. The cerebral change consisted in the extensive crushing of the front and lower portion of the right hemisphere where the surface was reduced to a greyish pulp. The adjoining part of the left hemisphere was also somewhat bruised. The medulla oblongata and posterior parts of the encephalon were examined with much care and found to be essentially natural.

The following case is from the same source:—

A farm labourer, 19 years of age, was, on October 26, 1861, struck on the right occipital region by the fall of a tree. This caused a wound of the integuments with fracture of the bone, loss of consciousness, vomiting, and general immobility without localised paralysis. On the 27th the urine was unnaturally abundant and contained five grammes per thousand of sugar. By the 28th the sugar had increased to six grammes. On the 30th the patient experienced an unnatural appetite and had symptoms of tetanus, the sugar in the urine having diminished. On the 1st of November he died. There was found to be a linear fracture of the occipital bone extending to the base of the skull. A minute examination failed to discover any injury to the cerebral substance.

Many other examples have been put upon record in which the urine has been found to be saccharine after fatal fracture of the skull. Dr. Pavy relates the following:—

A little girl four years of age had been run over in the street and was brought into Guy's Hospital. She lived four and a half

[1] Fischer, loc. cit., p. 422.

hours after admission. During this time she lay in a state of quiet unconsciousness without the power of swallowing. Her respiration was of a convulsive or sobbing but not stertorous character. A little blood ran from the nose and mouth. It was found after death that the skull had been fractured through the base and that the surface of the brain was slightly bruised. The fornix was slightly ecchymosed. Some ecchymosis was also observable upon the floor of the fourth ventricle from slight effusion of blood into the substance beneath. The ventricles contained a little bloody serum. A little blood was found on the outside of the dura mater, but the dura mater itself was not injured. The urine removed from the bladder at the post-mortem examination was found to contain sugar to the amount of $5\frac{1}{2}$ grains to the ounce. The urine was also slightly albuminous.[1]

In these cases the urinary change, though not always without constitutional symptoms, was slight and quite unimportant in the face of the severe injuries from which it sprang. It is conceivable that the glycosuria may have depended either on the rupture of nerve filaments, or upon injury to the tissue of the brain such as in the second case to elude observation. Cases to be presently mentioned will show that it is to lesion of brain rather than of nerve that we must assign the result.

Traumatic glycosuria not slight but transient.

Passing to such cases as are classed by M. Fischer as *transient glycosuria*—cases in which the urine contained abundance of sugar for a time varying from ten days to three months, the return of the secretion to the natural state coinciding with the disappearance of the cerebral disturbance—I may place first one which, as sometimes happens with truthful observations, finds its meaning in the future. It was related by Baron Larrey.[2]

In the year 1820 a fusilier named Lecœur, 22 years of age, received a thrust from a foil, from which the button had broken, through the inner wall of the right orbit backwards and to the left deep into the interior of the skull. On the morrow he was hemiplegic upon, and the tongue was pointed towards, the right side. He suffered

[1] Pavy 'On Diabetes,' 2nd ed. p. 190.

[2] The case is recorded by the elder Larrey in his 'Clinique Chirurgicale,' vol. i. p. 177.

from vertigo and obstinate constipation. Under venesections, cupping, sinapisms, and large doses of acetate of ammonia the general disturbance had by the nineteenth day passed off; the hemiplegia remaining, the intellect being unaffected save that the patient had lost the power of recollecting proper names. The sight of the right eye was peculiarly modified so that the patient could see with it only the horizontal half of objects before him.

Under moxas the hemiplegia diminished. Two and a half months after the accident, when able to walk about, he was suddenly attacked with diabetes, the urine displaying on analysis a great quantity of sugar. This Larrey attributed to the action upon the kidneys of the spirit of Mindererus, of which he had taken a large quantity. On the seventh day the saccharine condition of the urine disappeared.

Three months after the accident the patient while apparently convalescent was, after having been exposed to some cause of mental agitation, suddenly seized with headache and vomiting, followed by fatal stupor.

After death it was found that the weapon had entered the skull through the part of the frontal bone forming the inner and upper part of the right orbit, and thence penetrated deeply into the brain, its course being indicated by a canal containing coagulum. This involved first the inner and fore part of the right hemisphere and then entered the left, piercing it as far as the lower wall of the left lateral ventricle almost to the medulla oblongata. The root of the right optic nerve had been wounded near its origin. There was no trace of suppuration about the wound, but some pink serum was found under the brain and in the spinal canal.

The thrust which killed this soldier, more than half a century ago, with its noted accession and subsequent cessation of glycosuria, furnished almost as characteristic an example of sugar-puncture as could be found with any of the baser victims of modern physiology.

Subsequent to Bernard's experiments Dr. Goolden published some cases in point, of which the following may be cited:—

A railway guard, aged 46, was stunned by a blow on the side of the head from the handle of his break; but in an hour had sufficiently recovered to walk with the help of a man on each side to a house a mile off, where he was put to bed. He suffered from

concussion of the brain, having no recollection of the accident or how he got to the house. He recovered from all the urgent signs of concussion, and made an ineffectual attempt to resume his duties, but he was so much affected by the shaking of the train during a short railway journey, that he was referred to Dr. Goolden. It is not explicitly stated how long this was after the accident, but before its immediate effects had subsided. He complained of giddiness and of confusion, and of tenderness where the face had been bruised. It was learned that ever since the blow he had passed a most extraordinary quantity of urine, insomuch that at the cottage where he resided they could not get vessels enough to contain it till morning, as he filled all the chamber vessels and the washhand basin.

The urine on examination was loaded with sugar and had a specific gravity of 1,052. The skin was dry and harsh, the tongue red and sore; he had a large appetite and excessive thirst. His bowels were actively purged and his head blistered; measures to which Dr. Goolden attributes his recovery. Nature appears, however, to have effected some mechanical adjustment—possibly the replacement of some fragment of bone—which must at least share the credit; 'something in his head gave a click,' when he seemed to wake as from a dream, a cloud passed from his mind and the sugar from his urine. This fortunate crisis occurred within eleven days of his applying for advice, apparently not many days more remote from the accident.

For the following case I am indebted to M. Fischer's compilation. It was recorded by M. Plagge.

A boy of 16 received on the occiput a blow from a stick which did no obvious harm beyond causing a bruise. On the following night, however, he had strangury, which next day passed off. Three days afterwards he complained of dimness of sight, hunger, thirst, and excess of urine. The urine was pale yellow, faintly acid, of a specific gravity of 1,043, and loaded with sugar. The skin was dry and harsh. The pupils acted well, nor did ophthalmoscopic examination display anything abnormal. For the first week, during which he took opium and tannin with animal diet, the symptoms remained unchanged; in the following, while under bicarbonate of soda and ice, and the same diet as before, the symptoms gradually passed off. For two months, however, the urine, though free from sugar, remained superabundant.

The following case differs from the preceding in the fact that there was a recognised fracture of the skull:—

A man had a fall in which he received a fracture of the cranium with depression of the bone at the middle of the sagittal suture. On the day following the accident symptoms of diabetes declared themselves—urgent thirst, polyuria, and the presence of sugar in the urine. The glycosuria ceased spontaneously at the end of five weeks, at the same date that the other symptoms disappeared.[1]

These cases differ from the preceding series in the succession of the greater urinary change upon the lesser cranial mischief. Evidence of fracture was absent as often as not. We cannot but attribute the glycosuria to laceration, bruising, or interstitial hæmorrhage of the brain itself; and with the evidence which these cases afford—evidence which will be corroborated in the next class—we may presume that damage of brain rather than of nerve was the potential cause of the lesser degree of urinary change with the more complicated accidents.

Proceeding now to persistent glycosuria, a large number of cases might be collected, not differing in their symptoms or course from idiopathic diabetes which have ensued upon injury of the head.

Large and persistent glycosuria, or diabetes, as the result of injury.

The injury has generally been concussion without fracture, and a considerable interval has sometimes elapsed before the consequent symptoms have declared themselves.

M. Fischer has collected seven cases of this kind, of which I will give the leading particulars of three:—

A navvy received a violent blow upon the nape. Four months afterwards he was attacked with thirst, exhaustion, and diuresis, but the symptoms subsided under treatment. A year later he was found to present in a marked manner the general symptoms and urinary changes characteristic of diabetes, which continued as long as he was under observation.

A washerwoman fell upon her head with the result of a severe scalp wound and much hæmorrhage. Six months afterwards thirst, increased appetite, and the copious discharge of urine

[1] Related by Szolskaski, quoted by Trousseau, 'Sydenham Translation,' vol. iii. p. 494.

afterwards found to be of very high specific gravity, declared the presence of diabetes.

A farrier in good health was struck with an axe on the top of the head a little to the left of the median line. This was succeeded by difficulty in micturition, the urine passing in drops. These symptoms disappeared and were replaced by those of diabetes in so marked a shape that within a year of the accident he drank sixteen litres daily and urinated in proportion. The symptoms were complicated with hepatic disturbance, indicated by jaundice and tenderness in the region of the liver. He died twenty-one months after receiving the injury.

Dr. Pavy relates the following case:—

A cadet at Sandhurst, of 20 years of age, when in perfect health, received a violent blow upon the head from the ramrod of a piece of artillery with which he was practising. It knocked him down and rendered him for a while unconscious. He recovered from the immediate effects of the blow and went about in an ordinary manner; but, a few days after, symptoms of diabetes of a strongly marked character set in. When, shortly after the accident, he fell under Dr. Pavy's notice he was suffering in a severe manner from the disease.[1]

Diabetes in these cases—and the list might be greatly extended—ensued upon blows on the head without known breakage of bone. Fracture is not necessary, nor even helpful to traumatic diabetes; whence we may infer that the tearing of nerves is likewise unessential. The accident most apt to be thus succeeded is concussion, or, anatomically speaking, superficial comminution and interstitial hæmorrhage by *contre-coup*. By this means the brain may be extensively crushed or bruised by a blow which has caused no fracture. *Contre-coup*, the mechanism of which has never been fully explained, transmits the internal effect of a blow upon the skull to the brain surface diametrically opposite to the spot on which it was inflicted. Thus a blow delivered upon the top of the head may crush or bruise the brain at the base; and thus the medulla and the neighbouring parts where the glycosuric susceptibility

[1] Pavy 'On Diabetes,' 2nd ed. p. 190.

chiefly resides, none of which lie very far from the foramen magnum, are vulnerable from the vertex as well as exposed to such direct shocks as can reach them through the occipital bone.

Glycosuria from coarse morbid lesions of the brain.

In the preceding instances of traumatic glycosuria, where the blow was definite and sufficiently described—six in number—the part struck was the occiput in three cases, the vertex in two. In the sixth the blow was described as upon the side of the head.

Passing from the results of external violence to those of tangible disease, many instances might be adduced in which a transient or lasting saccharinity of urine has ensued upon intracranial extravasations, tumours, and masses of softening.

The following may serve as a connecting link between injury and disease:—

A patient was trephined for fracture of the right parietal bone. Six months afterwards diabetes occurred, then 'head symptoms,' *mouvement de ménage*, rotation of the body on the longitudinal axis, and at last paralysis of the pneumogastric. Death took place fourteen months after the accident. A fracture was found in the inferior occipital fossa with superficial softening of the cerebellum and its right middle peduncle.

Trousseau alludes to a case in which the exciting cause of glycosuria was found to have been a colloid tumour within the fourth ventricle.

Sir W. Gull communicated to Dr. Pavy the particulars of a case in which the same symptom arose in connection with apoplexy. A member of the medical profession, at the age of fifty-two, had a fit of this nature. He recovered from the fit but remained hemiplegic on the left side. Five weeks after the seizure the patient, who had never previously experienced any symptoms to lead to the suspicion of diabetes, began to undergo rapid emaciation. This drew attention to the urine, which was found to be loaded with sugar.[1]

[1] Pavy 'On Diabetes,' 2nd ed. p. 192.

Injuries elsewhere than of the Brain as Causes of Diabetes.

Besides blows on the head injuries of diverse other parts of the body have been succeeded by diabetes. Many of the accidents thus followed have been such as to affect the brain by indirect violence, as when a fall upon the feet from a height has caused 'head symptoms' expressive of fracture of the skull or contusion of its contents.

Fractures of the spine and blows upon the back and loins have been recorded in connection with transient or lasting glycosuria, injury of the cord probably forming the link. It has been experimentally shown that wounds of the cord, at least in the cervical region, may be productive of the urinary change in question.

More rarely violent muscular efforts, such as might conceivably have given rise to punctiform or interstitial hæmorrhage in the brain or cord, have been similarly followed; and cases have been reported in which the like sequence has been noted after injuries of the abdomen, especially upon the hepatic region. The liver is the instrument of diabetes, though the nervous system is usually the agent. The origin of glycosuria in injury directly inflicted upon this organ is consistent with the teachings of experiment, which have traced this result to puncture and other forms of artificial hepatic irritation (page 18).

Cases of diabetes which have a traumatic origin are few as compared with those for which no such cause can be discovered. Of Griesinger's 225 cases 13 only were traumatic—a proportion of 5·7 per cent.—one as large as common experience would suggest.

CHAPTER IV.

GENERAL SYMPTOMS AND COURSE.

THE beginning of diabetes is usually gradual. The patient while feeling otherwise well becomes habitually thirsty, and passes water increasingly, which excess he is apt to look upon as the result instead of the cause of his drinking so much. He loses flesh, but is reassured by keeping, or even augmenting, his appetite; and so insidious and delusive is the departure from health that it is long before he knows that he is ill. When he goes to a doctor his complaint usually is either of thirst, or dryness of the throat. Accession.

The urine, on the questions which such symptoms suggest, proves to be superabundant and to be persistently clear, notwithstanding that formerly it may have been often turbid with lithates. It is tested and found to be saccharine.

Sometimes the patient notices that accidental splashes of urine, which in health pass unnoticed, leave their record in white powdery spots, which are an incrustation of sugar.

The thirst, diuresis, and hunger increase with the disease, and the patient continues to lose bulk and strength. The skin of his face wrinkles and puckers as the subjacent tissues shrink, rather like the 'wet cloak ill laid up' than with the expressive lines of care and age. The surface of the body generally becomes dry and harsh, often scurfy or besprinkled with fine white dust. The hands rub together, as Pavy observes, with a dry sound, and the lines of flexure become opaque and mealy. Hectic Wasting.

night sweats, however, are not infrequent in the latest stages.

Other functions are deranged. The bowels are often obstinately confined. Feelings of indigestion, flatulence, eructation, and gastric uneasiness occur, and a peculiar epigastric pain is sometimes the precursor of death, especially I believe when the patient is under the influence of opium.

Eczema of genitals.

The contact of the saccharine urine may cause, if the sufferer be a female, an annoying eczema of the vulva which is peculiar to the disease and not seldom is the first sign by which its presence is recognised. More rarely in men the orifice of the urethra, or the glans, becomes inflamed or irritated. If the patient be a man and the disease severe, he may lose the power of erection and with it sexual desire, recovering both should the symptoms mitigate. Instances have been known in which confirmed diabetics have obtained the credit of paternity.

Impotence.

Mental deterioration.

The mind deteriorates morally and intellectually. The sufferer becomes drowsy and his wits sluggish. The disease supplies, like advancing age, 'fears to the brave and follies to the wise.' The strong and resolute character becomes weak and vacillating. The equable temper becomes fretful, irritable, and passionate; and the courage and constancy which once opposed a calm front to all the storms of fortune now yield to a querulous and tearful despondency.

In small matters, such as details of diet, diabetic patients are prone to deceit: they are sometimes crafty without purpose. I knew one who mixed his urine with that of other persons in order to convict them of the disease, which, when done, it was hard to see how he could profit by.

Breath.

The breath acquires a peculiar etherial odour. Sir Thomas Watson has likened it, not inaptly, to the smell of a place where apples have been kept. This characteristic scent is most marked when the bowels are confined;

it increases with the stress of the disease, and furnishes a rough measure of its severity.

Tongue, &c.

The tongue is often red; in some cases it is obstinately and thickly coated with white fur; latterly it is apt to become glazed and dry, or streaked with brown. The mouth, in severe or advanced cases, is clammy or sticky, and may give further annoyance by constantly tasting sweet. The tongue and mouth are most parched when the diet is without restriction. The gums, which are often somewhat sore or tender, shrink, especially if the patient be of declining years, so that the teeth become exposed at their roots, and thus loosen and fall out, anticipating the toothlessness of age.

With an unquenchable thirst and a ravenous appetite, the patient drinks water sometimes by pailfuls, and eats to almost as huge an excess; but he nevertheless continues to emaciate, his calves no longer fill his youthful hose, and he becomes feeble and tottering.

Dropsy.

The next step is to dropsy; one not always taken, but taken perhaps more often than not. The simple view that dropsy is the mere outpouring from the blood of liquid which owing to the closure of natural exits cannot otherwise escape, has no place here. It is almost surprising to see the legs filling while the kidneys may be discharging six times more than their due. I have known the lower limbs to become highly œdematous, and that without any venous obstruction to account for it, while the urine amounted to two gallons a day. Anæmia is probably the immediate cause of the œdema of diabetes, as of the œdema of starvation; and it is worth a parenthetical remark that, when in connection with diabetes, the symptoms may often be promptly removed by perchloride of iron. The oft-repeated phrase which reckons 'an incurable dropsy' among the terminations of the disease requires to be supplemented by another, to the effect that dropsy often occurs in its course and under treatment subsides before its close.

The œdema is soft and painless; it is usually confined

to the lower limbs. After its apparent subsidence traces can often be detected in the hollows about the ankles, and upon the tibiæ.

As the disease advances the patient complains more and more of feeling weak. The pulse becomes feebler and somewhat quicker; he moves little, dozes much, and complains of being chilly. Latterly his appetite fails, and the sugar and the urine lessen. He has no pain, and perhaps his chief discomfort arises from the dryness of his mouth. Boils and carbuncles often occur either spontaneously, or as the result of some superficial irritation, like a blister, which in health would not suffice to produce them. Prout gives it as the result of his experience that 'carbuncles and malignant boils, and abscesses allied to carbuncles,' are always accompanied by diabetes. This rule, however, appears to be by no means without exception.

Boils and cutaneous eruptions.

Prout thought that there was a connection between cutaneous eruptions and diabetes, the eruption in his view preceding the disease; but later observations have shown this association to be at least infrequent. Lichen has occasionally been noted in the course of the disease.

The cutaneous sensibility diminishes, appreciably to the æstheriometer, though not amounting to numbness of which the patient is conscious.[1] This may be due partly to the dryness of the skin, but probably in larger measure to the general blunting of the nervous faculties, mental and bodily, which belongs to diabetes.

Gangrene.

Gangrene, such as occurs in old age, is an undoubted though a rare complication. A connection between gangrene and diabetes was first pointed out, and has been since fully discussed,[2] by M. Marchal (de Calvi), and instances have been cited by Garrod, Trousseau, and others. The gangrene, in the great majority of instances, begins in a toe, whence it may spread to the destruction of a considerable part of the foot. It has been known to

[1] Dr. Laycock, 'Medical Times' for 1871, i. 570.
[2] 'Recherches sur les accidents diabetiques.' Paris, 1864.

originate in other parts of the lower extremity, and even upon the trunk, the neck, or the nose. It commonly begins with a small ulcer, from which sloughing ulceration or gangrene spreads. It may occur in sequence to boils or artificial excoriations. Sloughing has been known to follow a blister applied *secundum artem* to the back of the neck. The affection in its symptoms and progress closely resembles senile gangrene. It is usually a late though not always fatal complication of diabetes.

As to the mode in which the change is brought about observations are wanting. It has been attributed to a degenerative change in the arterial walls; but as against this view it must be urged that after death by diabetes disease of the arterial system is chiefly noticeable by its absence. Arterial degeneration, whether measured by atheroma or by cardiac hypertrophy, finds its maximum with albuminuria, and perhaps approaches its minimum in diabetes. The arteries in this disease are usually smooth for the time of life, and the heart smaller than natural. Apoplexy, a result and sign of vascular decay, is rare. The deterioriation is probably not in the arteries but in the blood; and the change either such impoverishment that it is no longer able to support the tissues, or an abnormal coagulability which renders it liable to block the small channels.

Albuminuria.

Among the later complications of the disease must be mentioned albuminuria. With diabetes of long standing the urine more often than not contains a trace of albumen, sometimes a considerable amount. When sugar and albumen are together, the sugar as a rule is primary, the albumen consequent. The kidneys, goaded by the diuretic action of the sugar, after a time show signs of irritation and allow a little albumen to escape as the result of congestion or tubal disturbance. After death the kidneys give evidence of this process in their increase of bulk, vascularity, and superabundance of epithelium (see page 57).

Beyond the trace of albumen the renal change is almost invariably without symptoms.

As an example of what was probably an accidental inversion of the usual sequence, I may mention a man forty-seven years of age who came to me with highly albuminous urine, and acute renal dropsy general and severe. He lost his dropsy and recovered apparent health. Four years later I saw him again with as marked diabetes, the symptoms of which had manifested themselves six months before. The urine now contained only a trace of albumen but was largely saccharine. There was probably no pathological connection between the two disorders.

Cataract, a late complication of the disease, one which touches not only comfort but life, by means of depression, loss of exercise, and possible surgery, must be put aside for subsequent consideration.

Termination in pulmonary disease.

In the later stages of the disease other localised troubles may occur. One of these, which is so frequent as almost to belong to the usual course of the disease, is a condition of pulmonary deposition and excavation which is not to be distinguished in its symptoms from a rapid form of tubercular phthisis, though there is reason to believe that it has no relation to tubercle.[1] With this are the stethoscopic signs of rapidly increasing vomicæ at the apices; profuse muco-purulent, and at last purulent, expectoration; loss of appetite, hectic night sweats, and hastened wasting. The sugar in the urine lessens and at last may entirely disappear, the secretion now, possibly for the first time since the beginning of the disease, depositing lithates. The absence of sugar from the urine in a case of this sort where formerly it had been abundant led me to look for it in the expectoration, which was profuse and purulent. I found none.[2] That sugar ceases to escape is probably due to its increased consumption in the body in association with pyrexia. It is often to be observed in the course of diabetes that the urinary sugar varies inversely

[1] See page 55.

[2] Trousseau states that the bronchial mucus secreted in diabetes contains sugar. Vol. iii. p. 506, Sydenham edition.

with the febrile state. The sugar lessens with any chance rise of bodily temperature, and with its fall increases.

The pulmonary consumption of diabetes appears, as elsewhere shown, to be a form of chronic pneumonia; and inflammatory affections of the lung in more ordinary shapes sometimes bring about its end. Though fatal they are often latent; more obvious after death than in life. Fatal œdema of the lung, marked by general coarse crepitation and rapid sinking, is not unusual.

Other fatal chances beset the course of diabetes. The sufferer lives, as Prout has expressed it, on the brink of a precipice. Slight causes may suffice to loosen his feeble grasp of life. He may quietly subside into the grave from the want of the power to rally from some small injury or trivial operation like that for cataract, or even from the fatigue of a journey, or some depression of mental origin. He may sink, almost unexpectedly, from some complaint like influenza, which to previously sound persons would entail no danger.

By exhaustion from some apparently inadequate cause.

If the diabetic patient by luck or pace has escaped the dangers of the road, he finds the end of his journey in incomplete or complete coma. A lethargic and drowsy condition slowly advances into unconsciousness, and the unconsciousness deepens into stertor and death. There is no definite or limited paralysis; the state nearly resembles cerebral uræmia. It has been attributed to poisoning by sugar, and probably with reason, since no change in the solid structures is found to account for its accession.

In coma.

The preceding sketch is of diabetes in its severe and typical form as it occurs in early and middle life, and exceptionally in old age. The symptoms range from those depicted to absolutely none, save the presence of a small quantity of sugar in the urine. The younger the patient the more urgent the symptoms and the more rapidly fatal the disease. In advanced life the disorder is often mild, intermittent,[1] and well-nigh harmless. A little sugar may

Slight and intermittent forms.

[1] Instances of intermittent diabetes have been recorded by Dr. Bence Jones in the 'Medico-Chirurgical Transactions' for 1853, vol. xxxvi.

be found at one examination and at another none, owing either to restriction of diet, or to apparently spontaneous fluctuation.

With corpulence.

With corpulent people also, who seem rather prone to the disease, it takes a form of little severity. Perhaps their accumulated fat—store laid up against the evil day—enables them to withstand an expenditure which would dangerously impoverish them had they less personal property to draw upon. Prout mentions a gentleman weighing twenty-seven stone who became subject to diabetes for a time; then under diet and the baths of Aix-la-Chapelle exchanged sugar for uric acid, and was seen five years afterwards apparently well.

Slight and severe cases may differ only in degree.

All the types of diabetes referred to in which the excretion of sugar is for a long time constant, or at least constantly repeated, would seem to be no more widely different than as degrees or stages of the same disease. Symptoms which are wanting at one time may show themselves at another; mild cases gravitate, and occasionally severe ones assume under treatment less threatening characteristics. It has been sought to establish a distinction in kind between the more and the less severe forms of the disorder; the less severe form with little wasting has been described as *diabetes from excessive formation*, and attributed to the increased making of sugar in the liver; the more severe form with much wasting has been described as *diabetes from diminished assimilation*, and attributed to diminished appropriation of sugar by the tissues.[1] The distinction, however, is hypothetical, and can scarcely be regarded as probable. That sugar is sometimes made in excess is certain; but it may be doubted whether its accumulation and escape is ever due to its being thus repudiated by the tissues. And clinically we cannot trace any line of abrupt separation to indicate such a division.

A demarcation, somewhat shifting, but of practical value as affording a definite standard of severity, may be made by dividing the cases in which sugar is only trans-

[1] The Urine and its Derangements.' Dr. George Harley, p. 259.

mitted from those in which it is developed. In the former the sugar ceases from the urine when saccharine and amylaceous matters are withdrawn from the food; in the latter not only are such matters voided as sugar, but sugar is made in the body out of the protein compounds, insomuch that restriction of diet lessens but does not prevent its excretion.

Sugar sometimes only transmitted.

Sometimes developed.

The typical subjects of the first form are plump and rosy; those of the latter are thirsty and lean. The first class comprises early, slight, intermittent, and possibly protracted cases which involve little loss of flesh or warmth and no obvious impairment of the general health. The second class, often the sequel of the first, includes the graver types of the disease, from which the classical descriptions have been drawn, with irrepressible diuresis, marked lowering of temperature, and failure of nutrition. There is no reason to suppose that the contrasted conditions differ more than as distant links of the same chain; they are apparently produced by similar external causes, and benefit by similar treatment, modified by the circumstances of each. The slighter cases may not require, the more severe and immediately threatening may not endure, as rigid restriction of diet as is beneficial in the intermediate conditions.

The same case often passes through both phases which must be regarded as merely different degrees of the disorder which may be termed nervous diabetes, or diabetes proper.

Of this the liver is the agent, the brain the instigator. But clinical experience suggests that there is a form of glycosuria which is primarily hepatic. It is slight and transient, and without much diuresis. It occurs in full-fed, gouty, and plethoric persons whose urine is loaded with uric acid or lithates, and ceases under purging and abstinence. In this form of glycosuria the constitutional symptoms of diabetes are mostly absent.

Hepatic glycosuria.

These views are to a certain extent speculative, having only the basis of such experience as can be gathered from

the living. I never examined the nervous centres after the comparatively unimportant glycosuria to which I have referred, nor knew such a case to be fatal.

The following may serve as an instance of its occurrence :—

Case. A wine merchant, 47 years of age, largely his own customer, experienced an unwonted desire for aqueous liquids, and drank to the extent of 6 pints in the twenty-four hours. After six weeks of this he applied to Mr. Venning, who found sugar in the urine, and asked me to see the patient. The man had a full habit, a tremulous manner, a blotchy, turgid complexion, spots of purpura on the legs and lower parts of the body, and yellow conjunctivæ. The liver could not be felt below the ribs. The urine deposited much uric acid; it had a specific gravity of 1,019; it contained albumen coagulating to one sixth, and sugar decidedly but not abundantly. He was told to abstain from alcohol in every shape, to take air and exercise, to limit himself to a plain diet exclusive of potatoes and bread, to take nitro-hydrochloric acid and strychnia, with repeated purges of calomel and senna. The purpura rapidly faded, he became less puffy, the eyes cleared, and in a fortnight the sugar ceased from the urine. He speedily resumed his former health, which under temperance and Vichy water he maintained; the urine remaining slightly albuminous but no longer superabundant and without a trace of sugar. The patient was then allowed to take amylaceous food without restriction, and without recurrence of the glycosuria.

It could hardly be doubted that the sugar in this instance appearing with evidence of hepatic engorgement, and removed by abstinence and purging, had its origin as well as its immediate source in the liver. The case should not be termed diabetes, with which disease it has but little in common, but rather hepatic glycosuria.

Possibly in consequence of hepatic embarrassment, primary or secondary as the case may be, an excess of uric acid is by no means infrequent in association with the excretion of sugar. The liver is known to be concerned in the disintegration of albuminous matter, and its partial conversion into urea. Hepatic disturbance especially of the congestive kind appears to render this so far incom-

plete that urea is to a certain extent replaced by uric acid. There are few clinical observations better attested than the connection between lithatic deposits and hepatic congestion. And their origin in not dissimilar states of the same organ may account for the concurrence of lithiasis and glycosuria. It has been observed that the urates often precede sugar in the urine.[1]

This sequence has fallen in with the notion that uric acid and sugar merely mark different stages of insufficient oxidation. But if I am right in presuming from the observations which I have already stated, that glycosuria when persistent is the result of structural organic change, we must regard this theory of abstract chemistry, or of chemistry from which organic influences have been abstracted, as insufficient.[2]

To this general sketch of the symptoms I will add some particulars which relate to the bodily temperature, and to the changes wrought by the disease within the eye.

TEMPERATURE.

In uncomplicated diabetes, the temperature of the body is depressed somewhat in proportion to the gravity of the disease.

In a case of extreme severity in a boy of 6, the temperature commonly varied from 93·6 to 94·8; on the approach of death, the immediate cause of which was pneumonia, the temperature reached the elevation, with this patient unprecedented, of 97·8.[3]

A youth of 18, who passed at one period more than two pounds of sugar a day, had a temperature which ranged from 96 to 98·6. On the occurrence of excavating pnue-

[1] See Dr. Murchison's 'Lectures on Functional Derangements of the Liver.' 'Brit. Med. Journal,' 1874, p. 471.

[2] Touching the association of sugar and uric acid, it must be borne in mind that the power which this acid has of reducing sugar may lead to error when only the copper test is used.

[3] Hatcher, plate I.

monia, however, the heat of skin became irregularly high, reaching a maximum of 103·2.[1]

A woman of the age of 35 who had the disease less severely and without pulmonary complication, had a temperature which varied from 98 to 100·3; no marked depression. Within four days of death, however, the thermometer fell to 94·4.[2]

A man, 68 years of age, at present under my care, who has the disease in the slow form belonging to his time of life, has a temperature which ranges from 95·8 to 98·4.

The general lowering of temperature is probably due to the loss of the material the oxidation of which is a source of heat. With the uncomplicated disorder a marked fall of temperature may foreshadow the end. The pulmonary complication may, as seen in the instance quoted, be attended with febrile action which will not only recover the normal temperature but for short periods far exceed it.

I might quote similar observations upon a number of other diabetics; but without adding to the information given, since in all the temperature has varied in the direction and within the limits indicated.

Affections of the Eye consequent upon Diabetes.

Cataract. Cataract has long been known as an accompaniment of diabetes. Dr. Prout noticed it in two instances, in one of which an operation was successfully performed, and other writers, foremost among whom is Mr. France, have since established that the concurrence of the two disorders is too frequent to be accidental.

Among the 225 cases of diabetes brought together by Griesinger, were 20 of cataract, or about one in ten. Bouchardat places the proportion at one in 38; the lesser frequency corresponding more nearly with English experience. Dr. Roberts found one instance in 45 cases. Among 28 persons who died of diabetes in St. George's Hospital one had cataract.[3]

[1] Howel, p. 144. [2] Ann Mackay, p. 165. [3] See case of Kirby, p. 155.

The complication occurs late in the disease, and often marks the beginning of the end. It usually affects both eyes, either simultaneously or in succession; when in succession, the right eye usually suffers first. The opacity, when commenced, is soon complete, not seldom within a week. In a case under my own notice the process, however, occupied several months. The cataract is generally soft, though with elderly persons it may be firm, and may contain a hard nucleus.

Mode of its formation.

Light has been thrown upon the pathology of diabetic cataract by the interesting observation of Dr. S. Weir Mitchell, that the administration of sugar to frogs caused their lenses to become opaque; the opacity ceasing after the animals had been for a time in water and presumably eliminated the sweet poison. I will quote one experiment among many related by Dr. Mitchell.

'About two drachms of syrup were injected under the skin of a large frog. In twenty-four hours the lens was opaque, and, as the animal appeared lively, it was placed in water, in order to test the permanency of the opacity. Ten hours in the water sufficed to remove most of the opacity from the lens, which began to clear in the centre first. Twenty-four hours after the frog had been placed in water the eyes were perfectly transparent, and the animal himself entirely well.'[1]

Dr. Mitchell found that the same condition of the lens could be brought on after its removal from the animal by soaking in syrup, and inferred with apparent reason that the opacity was due to an alteration in the tubes from osmotic action. Dr. Richardson[2] subsequently confirmed Dr. Mitchell's statements, and found that the same result could be produced by the injection of a great variety of saline and other solutions, having a specific gravity above 1,095, or, in other words, greater than that

[1] Dr. Weir Mitchell. 'American Journal of the Medical Sciences,' 1860, p. 108.

[2] The Synthesis of Cataract. 'Journal de la Physiologie.' Par Brown-Sequard, 1860.

of the blood, their specific weight being apparently the one thing needful to the production of the opacity. Solutions of iodide of potassium for some unexplained reason were exceptional, insomuch that however concentrated they caused no change in the lens. These experiments explain the formation of diabetic cataract. The fluids of the lens pass by exosmosis to the unnaturally dense blood without; and the density being continuous instead of, as in the experiments, only of short duration, time is afforded for the precipitation within the lens of calcareous and other matters to its permanent injury.[1]

Danger of operation.

Surgery in such cases is attended with unusual danger, first, from the consequent suppuration to which diabetic subjects are especially prone, and, secondly, from the likelihood that even if the wound heal well, the patient may be dangerously depressed by the successive action of apprehension before the operation and darkness and restraint after it. In an instance within my own experience the patient sank after an operation for cataract which locally was perfectly successful. It has sometimes happened, however, that the proceeding has been in all respects satisfactory, though the perils which environ it are such as to justify its performance only in exceptional circumstances.

Long-sightedness.

Other defects of vision occur with diabetes, one of which is premature and rapidly increasing long-sightedness.

Temporary or variable dimness of sight is often noticed, due, as has been supposed, to want of adjusting power owing to the failure of the ciliary muscle. In these circumstances Dr. Pavy has found benefit from the application of Calabar bean.

I have been frequently indebted to my colleagues, Mr. Power and Mr. Brudenell Carter, for examining diabetic patients with the ophthalmoscope; they have in most instances reported dilatation of the retinal vessels, more

[1] A full account of diabetic cataract is given by M. Marchal (de Calvi) in his 'Recherches sur les Accidents Diabetiques.'

especially of the veins. In one instance only anæmia of the retina was noted. A more profound change, atrophy of the optic discs, with consequent hopeless amaurosis, has been found often enough with diabetes to show that it is pathologically connected with it. I have not chanced to light upon any example of this state. It must be surmised that it is but a part of the nervous deterioration which lies at the root of the disease.

Amaurosis.

Besides consecutive atrophy of the retina and optic nerve, retinal hæmorrhage like that of albuminuria has been found in association with diabetes. It has been thought that possibly in such cases the urine may have contained both sugar and albumen, and that the retinal hæmorrhage was especially associated with the latter. It is by no means improbable, however, that the hæmorrhage in such cases is essentially diabetic. It is true that with diabetes we find no such general vascular change as occurs with the granular kidney, and no general liability to rupture and hæmorrhage. But minute cerebral extravasations are common with diabetes if not essential to it; and it is likely that the loss of arterial tone which allows transudation of blood within the brain may exist and produce the same result in the retina, which is but an outlying part of the brain. Dilatation of the retinal vessels as seen with the ophthalmoscope is indeed, as already stated, common with diabetes.

Retinal hæmorrhage.

Duration.

There are few disorders of which the duration is more various than is that of diabetes; it is not possible to limit its period more narrowly than by saying that with rare exceptions it is a chronic disease. As a rule the later it begins the longer it lasts; and sometimes, especially when it is intermittent, and also occasionally when it is not, it allows of the attainment of so respectable an age that it would seem scarcely to have hastened the inevitable hour. Griesinger,[1] in the table I have transcribed, has

[1] 'Studien über Diabetes,' p. 49.

given the duration of the disease in 100 cases collected by him; and I have placed by its side a corresponding statement with regard to 25 cases which ended fatally in St. George's Hospital.

	St. George's Hospital	Collected by Griesinger
Under . . ¼-year	1	1
Between ¼ and ½ "	2[1]	2
" ½ " 1 "	8	13
" 1 " 2 "	6	39
" 2 " 3 "	5	20
" 3 " 4 "	1	7
" 4 " 5 "	0	2
" 5 " 6 "	0	1
" 6 " 7 "	0	2
" 7 " 8 "	0	1
Undetermined . .	2	12
	25	100

General duration.

It may be stated with general truth, that diabetes rarely kills under six months; that in a large majority of instances it does so between six months and four years; but that the time over which it occasionally extends is scarcely limited but by the natural ending of mortality.

Sometimes apparently acute.

Death has sometimes occurred shortly or almost immediately upon the detection of the complaint, but its progress has obviously in most such instances been occult rather than acute. A man was brought into St. George's Hospital dying with diabetic coma in whom no symptoms of the disease had previously been noticed. The disease was undiscovered but not necessarily acute. Putting aside this case, and reckoning only those of which the history was fairly complete, the experience of the hospital affords no instance of diabetes fatal within six months of the first symptom. 'Acute diabetes,' however, is occasionally recorded, and we may be content to believe that in some instances the course of the disease, whether latent or not, has

[1] In both these instances death occurred at six months.

been exceptionally hastened. Dr. Bence Jones[1] relates under this denomination the case of a gentleman 35 years of age, who died the day after the nature of his ailment was discovered after only six weeks of observable diuresis. Dr. Noble[2] reports two similar cases of diabetes, fatal almost immediately upon its detection; but it is impossible to draw any inference in either as to how long the urine may have been saccharine. Constitutional symptoms had been observed in one case for 'a few,' in the other for 'some' weeks. Dr. Roberts saw a child of three years who died in three weeks.

Case of ostensibly acute diabetes.

The following case of the disease, either acute or else presenting a rapidly fatal aggravation of a form so slight as not to affect health or attract notice, was communicated to me by my friend and former teacher, Dr. Paget, of Cambridge, in whose practice it occurred.

The patient was an undergraduate in whose family diabetes was hereditary, though I could not learn in what degree. 'He was,' says Dr. Paget, 'a steady man. He was the only son of a widow and the heir, or actual possessor, of large means. His mother lived in ———, at the West End of London. I mention these facts to show that, *if* the disease *had* existed some time, it was strange that it should have had no treatment or notice of any kind. He was about 20 years old. He had recently been on a short walking tour in Wales,' (which it appeared he had taken under advice in consequence of having been troubled with boils, very common annoyances among Cambridge undergraduates;) 'and still more recently—a few days before I saw him—had been engaged in the foot races of his college. He had not won any prize, but had run second in one or two of the races. I saw him in consultation with Mr. Bumpsted, who had been attending him only a day or two, not longer than two days at the most. When I saw him on the 23rd (of March 1870) he was in a state of half consciousness, quite unable to give any account of himself, lying on his back and looking somewhat like a man in an advanced stage of typhoid fever. I was puzzled at first. There was no urine then to be had for examination. On going close to him I smelled his breath, which plainly exhaled the diabetic

[1] 'Lectures on Pathology and Therapeutics,' p. 52.
[2] 'British Medical Journal,' 1863, January 17.

odour, and in an hour or two afterwards I obtained some of his urine and found that it was highly saccharine. The stupor passed into coma, and he died on the night of the 24th.

'His mother and sisters were wholly unaware that he had been ill. He himself could scarcely have thought himself ill, under such circumstances as I have already mentioned. Moreover, I learned from his bed-maker that during the three or four days before his death she had carried out of his bedroom enormous quantities of urine—a slop-pailful or more per day—and she had never noticed until the last few days that he had passed an unusual quantity. The case *may*, perhaps, have been one of extraordinarily acute diabetes, but the evidence is deficient in the precision and certainty which would quite justify a conclusion contrary to general experience.'

I have learned from Mr. Shann, his victor in the race, now a student at St. George's, that he ran a mile race on the 11th of March, twelve days before his death, confidently expecting to win, and much dejected by his coming in second. He seemed to be then in perfect health. A few days afterwards he walked with a friend to some coprolite pits near Ely, and spent some time searching for fossils up to the ankles in water. In the evening he felt ill, but the next day practised running as usual. When next seen by his associate he was lying on a sofa, with a bowl of lemonade by his side, very disconsolate about the race.

Subsequently Dr. Paget learned from an old family nurse that her young master had been a 'thirsty lad,' drinking much water; this, together with the boils, would warrant the impression which Dr. Paget tells me he received from the case, that it was an instance of diabetes so mild as not to have attracted attention until suddenly aggravated.

How mild, if indeed existent, is shown by the athletic and apparently healthy state of the patient to within twelve days of his death.

Probable pathology of acute diabetes.

It is by no means unlikely that in some such cases as have been referred to, death may really ensue very briefly after the outset of the disease. Diabetes sometimes begins with sudden and severe symptoms and much constitutional disturbance, both the special and general manifestations lessening and quieting by mere lapse of time. We can easily believe that the first stage may, when of exceptional

severity, be fatal. We may with probability associate the violent outbreak with generally scattered points of cerebral hæmorrhage, such as in greater or less number have been shown to belong to the beginning of the disease. It is not unlikely that death may now and then occur in the first hæmorrhagic stage, should the minute extravasations be more than commonly numerous and general.

Occasional extreme chronicity of diabetes.

With regard to the protraction of the disease we have more certain knowledge.

Prout knew of but one instance in which the disease was clearly ascertained to have lasted ten years. His experience, however, is carried on by Bence Jones, who tells us of a diabetic clergyman, alive in good general health, though Prout had discovered sugar in his urine sixteen years previously. In this instance the disease was intermittent; and the patient had two brothers, both of whom had it in a similar interrupted and protracted form.

And as an example of similar protraction of the complaint, though in its ordinary and constant shape, I may supplement the experience of Bence Jones, as Bence Jones has supplemented that of Prout, and cite the case of a tavern-keeper, now fifty-four years of age, whom I occasionally see. His disease began with marked symptoms fifteen years ago. He was at that time put by Bence Jones upon diabetic diet, to which he has kept since with creditable though not absolute strictness. He now passes about 100 grammes of sugar daily, and is in fair general health. He has been under medical observation during the whole course of his disease, and the urine, as I am informed by his attendant, has always contained sugar.

CHAPTER V.

URINE.

THE continued presence of sugar in the urine is pathognomic of diabetes. The escape of the sugar involves the issue of an increased amount of water, so that the bulk of the urine is increased in some sort of proportion to the amount of sugar discharged.

It is uncertain how far the increase of water is due merely to osmosis towards the escaping sugar, and how far to central nervous irritation, similar to that which causes the glycosuria but independent of it. Probably both influences act. The influence of the nervous system in causing hydruria, independently of glycosuria, is seen in the phenomena of diabetes insipidus; and in diabetes mellitus such variations sometimes occur between the proportions of water and sugar as would seem to indicate that separate influences bear upon each.

The diuresis and the thirst due to the dehydration it involves are commonly the first symptoms of the disease.

General characters of urine.

With its increase the urine early loses any habitual turbidity or lateritious deposition, and becomes bright and clear, acquiring a faint greenish tint and a peculiar odour, which is less marked than that of the breath, and has been likened to that of lactic acid fermentation. The urine, though clear of lithatic salts, may deposit crystalline uric acid, which it does in some cases abundantly. It attracts flies; where sprinkled it encrusts. It resists ammoniacal decomposition, but is found, especially in warm weather, to acquire a vinous odour, and deposits at the same time a bulky white sediment consisting of the sporules and fibres of the yeast plant. It is stated to possess a sweet taste; an assertion which may be accepted without verification.

Whether or not we accept the probable theory of glycogenesis by the division of albumen into sugar and urea, the urea increases in diabetic urine much in proportion to the sugar it contains. Sugar, as already shown, involves excess of urinary water, and excess of water involves an increase in many other urinary elements which are found to be more or less increased when in any way the flow of aqueous fluid is enhanced. Increased drainage carries out of the body more of its soluble constituents, as is shown by the effect of liberal water-drinking in an increase of many if not of all the solids of the urine. Thus with the urine of diabetes, not only is sugar superadded, but certainly most, probably all, of the natural components of the secretion are exaggerated. The exaggeration, however, is usually evident only with regard to the amount discharged in a given time; a given quantity of urine from superabundance of water usually contains a diminished proportion of everything else.

Observations to be of value must relate to the period of 24 hours—a rule which has been followed in the ensuing statements. The subjoined table shows the amounts of the urinary constituents in several cases which I have thought it unnecessary to detail, while similar observations are given with the notes of Kirby, Mackay, James and Joseph Howel, and others.

WATER.

Average of water in health 1500 c.c. or 52 ounces.

The urinary water, or, in other words, the amount of urine, is increased with the severity of the disease. From its normal amount, which may not be exceeded if the quantity of sugar be small, the urine ranges up to about 30 pints in the 24 hours. A hospital patient of mine[1] made in one day 532 ounces, or more than 26 imperial pints. Another,[2] a boy whose case is related, made 23 imperial pints. Sir Thomas Watson tells us that he has known 26 pints to be passed in the same time. Dr. Pavy

[1] Case of Salisbury, referred to with Plate I.

[2] James Howel, p. 144.

ANALYSES OF DIABETIC URINE FOR TWENTY-FOUR HOURS.

(*Grammes and Centimètres.*)

Name	Age	Nature of Attack	Quantity	Sp. Gr.	Sugar	Urea	Proportion of total Urea to Sugar, 1 to —	Proportion of excess of Urea to Sugar, allowing 3 grammes to a stone, 1 to —	Albumen	Phosphoric Acid	Sulphuric Acid	Chlorine	Salts of Alkalies	Salts of Earths	Lime (CaO)	Magnesia (2MgO)
			cc.		gram.	gram.				gram.	gram.	gram.	gram.	gram.	grammes	grammes
Thomas Jones	—	Not severe; under mixed diet.	3360	1028·6	224 V	42 V	5·3	13·0 ?	0	1·5 V	2·25	4·43	12·02	·920	·115 A	·098 A
Thomas Green	—	Improving; under ordinary diet; weather very hot.	1000	1028·7	15 V	26 V	·57	—	0	2·3 V	1·48	—	11·29	2·49	·408 A ·423	·26 A
Henry Reynolds	58	Not severe; under ordinary diet; before treatment; urine deposits uric acid.	1260	1028·8	56 V	27 V	2·0	—	0	1·2 V	1·28	2·49	7·54	·869	·109 A	—
Henry Reynolds	58	A month later, after diet and strychnia.	1250	1018·2	3 V	—	—	—	0	—	—	—	—	—	·354 A	·091 A

A tavern-keeper	51	Not severe; of thirteen years' duration; under partially restricted diet.	3090	1027·3	119 v	64 v	1·8	3·8	trace	3·0 v	—	—	—	—	·488 A	·216 A
Mrs. A—— .	56	Slight; diet partially restricted.	1450	1015·5	29 v	18 v	1·6	—	trace	—	—	—	—	—	·185 A	·087 A
Mrs. A—— .	56	Three weeks later, under diet and strychnia.	—	—	3 v	—	—	—	—	—	—	—	—	—	—	—
Captain H——	29	Severe, with much attenuation; strict diet, gluten bread, but no medicine.	4260	1030·0	213 v	—	—	—	0	5·1 v	—	—	—	—	2·227 A 2·19 [1]	·33 A ·37 [1]
Ann Nicholls .	34	Moderately severe; uncomplicated; mixed diet; no medicine.	1370	1039·0	91 v	39 v	2·3	5·1	0	2·7 v	—	—	—	—	·774 A	·143 A
Mr. D—— .	43	Severe; patient very corpulent.	2950	1034·0	184	38	4·8	?	trace minutest	1·03 v	4·27	5·7	15·5	4·03	·98	·44 (Uric Acid ·427)

v = estimated by volumetric process. A = estimated from ash. [1] Second estimation precipitated directly from urine.

ascertained that as much as 32 pints were produced within as short a space by a man in Guy's Hospital, and it would be easy to cite, though on less satisfactory evidence, examples of still more liberal urination. A labourer whom I remember in St. George's Hospital told Dr. Bence Jones that his water ebbed and flowed; the flow being seven gallons, the ebb five pints.

Passing from exceptional to daily experience, it may be said that in diabetes the urine commonly varies from the normal average which, for the male adult, is about 1,500 c.c. to 6,000 or 7,000 c.c. The amount is always to be controlled by diet; the examples of enormous diuresis being afforded by persons whose food is unrestricted.

It was formerly supposed that in diabetes the urine often exceeded the drink—that more water escaped by the kidneys than had been received by the stomach. Thus either water was absorbed from the atmosphere, or else, as was suggested by Lavoisier, the diabetic person, like the electric jar of Cavendish, possessed the means of combining oxygen and hydrogen introduced otherwise than in hydrous shape, and of making water in a sense more literal than is commonly attached to the phrase. Diabetic patients, however, are prone to deceit, and will often allay their thirst surreptitiously. And furthermore, it has been found, in cases noted with trustworthy care,[1] that the quantity of urine, if estimated for a considerable time, always falls slightly short of the amount of water introduced in liquid and solid food. It appears, however, that in diabetes drink makes its exit less promptly than in health, so that error may arise, if the observation be limited to a short period.

Specific Gravity.

Since the urinary water increases with the sugar, the specific gravity of diabetic urine is less altered than its quantity. It rises from its natural degree up to 1,074, in

[1] Parkes on the Urine, p. 340.

the majority of instances not passing below 1,025, or above 1,045. In exceptional instances the specific gravity falls below the average of health. Prout found it once as low as 1,010 ; and I might instance a case in which it fell to 1,008. In such cases the urine is prone to vinous change, and it is probable that in some there is loss of sugar by spontaneous fermentation.

Sugar.

There is reason to suppose that grape sugar is a normal constituent of urine, but in so minute a proportion as to be ordinarily inappreciable. The presence of this substance in such quantity as to affect rough tests is the special characteristic of diabetes.

In this disease the sugar varies from a trace only to be found at intervals, and perhaps then not exceeding two or three grammes in the twenty-four hours, to a daily manufacture of several pounds. A patient of mine passed 50 ounces in 24 hours; at which rate he would have made his own weight of sugar within the ecclesiastical period of 40 days. His rule of life, however, which was one of unbounded indulgence, savoured less of fast than of Carnival.

With restriction the sugar fell to 8 ounces. James Howel, whose case is related elsewhere, passed on his admission 917 grammes, or 32 ounces of sugar. This was successively reduced by dietetic and medicinal treatment, further diminished with the advance of pulmonary disease, and finally on the approach of death disappeared.

The liberal production of sugar, of which these cases are examples, is exceptional. If the sugar reach 500 grammes, or rather more than a pound daily, the case is one of rare severity and is probably unmitigated by diet. In a large majority the sugar never reaches half this amount, and probably a hundred grammes, or about 4 ounces, would more often than not exceed the daily yield : this would certainly hold good with cases under restricted diet. The urine is most saccharine about three hours

after food, least so during fasting. It diminishes with the withdrawal of starchy and saccharine matters from the food, and in cases of mild type or in an early stage, may with their complete abstraction entirely disappear. When not able entirely to get rid of the sugar by such means, I have more than once reduced a considerable daily secretion to three grammes or thereabouts. The sugar lessens under pyrexia. Towards death it usually diminishes, and sometimes, as in the instances referred to, entirely disappears.

Urea.

The belief of the older observers, that in diabetes the secretion of urea is lessened, or even altogether abolished, is contradicted by modern experience.

Average in health 33 grammes.

The amount of urea appears, if altered, to be always increased. Where the disease is severe the increase is enormous. The boy Howel (page 144) passed in twenty-four hours 142 grammes of urea, which was probably more than six times as much as he would have done in health. This was an extreme instance; but among the cases here reported are not a few in which the urea is double or treble its proper amount. The increase of urea in diabetes has been attributed to the large amount of nitrogenous food taken; but it is probable that this rough explanation may admit, to say the least, of some refinement. The urea and the sugar increase and diminish together with sufficient regularity to enable us, after the application of some necessary and obvious corrections, to discern a proportion between the two which is less variable than would probably be the case were they quite independent in their formation.

When sugar is elaborated from the protein compounds, as it must mainly be when under a diet exclusive of sugar and starch it finds its materials in animal food or the animal frame, we cannot but call to mind the theory of Haughton, that sugar and urea are the two fragments of

broken albumen. If not discharged as urea we are at a loss to know what becomes of the nitrogenous residuum after the abstraction of the saccharine hydrocarbon from the compound pabulum.

Professor Haughton has shown that, theoretically, protein, with the addition of small quantities of water, oxygen, and carbonic acid (which all exist in abundance in the blood), may become converted into glucose and urea in the proportions by weight of nearly 5 grains of glucose for every grain of urea;[1] and examining with certain allowances a considerable variety of examples of the disease, it is scarcely possible to doubt that, whether or not this represents the process with perfect accuracy, yet that something of the kind occurs.

According to this theory, albumen is put into the mill, sugar and urea come out; and, like the flour and the bran, wax and wane together.

To exhibit this result:—in the first place, all starchy and amylaceous food must be withheld, such matters, in severe cases at least, running off as unassimilated sugar, and disproportionately increasing the saccharinity of the urine.

In the next place, the proportion must be held to relate not to the total urea, but to its excess above the normal. Independently of sugar, urine contains as much urea as results from the processes necessary to life, alike in health and in diabetes. With this normal discharge no sugar escapes; the elements of sugar once associated with it are consumed in the nutrition of the tissues or the maintenance of heat. These processes can only cease with life; they take place in diabetes as well as in health. Hence every man, whether diabetic or not, discharges a certain amount of urea without any counterpoise of urinary sugar. It is only the excess of urea over this necessary amount which can be supposed to have relation to the sugar which is simultaneously discharged; and this,

[1] 'Dublin Quarterly Journal,' November 1861, p. 268.

according to chemical theory, should give a proportion by weight of 1 to 5.

Some observers, seeking to establish a constant ratio between the urea and the sugar without any deduction on the score of necessary urea, have thought that 1 to 2 expresses the proportion; but a glance at the cases here given will be enough to show that no such law holds. The urea may, when the sugar is in minute quantity, outweigh it many times told; on the other hand, the sugar may, even under diet rigidly restricted, amount, as in the instance of James Howel, to more than four times the weight of the total urea. And the two substances may bear to each other any proportion between these extremes.

If now we deduct as much urea as the individual is entitled to independently of diabetes, and compare the excess only with the sugar, we find, not indeed absolute uniformity of proportion, but quite sufficient regularity to indicate that the urea and sugar are mutually dependent, or are dependent on a common cause. It is, of course, impossible, since we cannot allow for individual peculiarities and varying circumstances, to determine accurately how much urea is, independently of its production in diabetes, due to each person; but taking the healthy average as three grammes in twenty-four hours to a stone of body-weight, and deducting urea at this rate from all alike, we shall obtain perhaps as good an approximation to the diabetic excess as is within cur reach. Possibly could we gauge the normal urea with individual exactness, we should find the relation of its excess to the sugar still less variable than the ensuing statements represent.

Taking instances where the diet has been as nearly as practicable exclusive of starch and sugar, I find that with Kirby, while thus restricted (see table, page 160), though the daily sugar ranged from 237 grammes to 61 grammes, the ureal excess varied with it so exactly as scarcely to depart from the ratio of 1 to 6·1. One day was exceptional,

showing a proportion of 1 to 4·1, but this was the farthest departure from the rule.

Vegetable or mixed diet increased the sugar so that the proportion became 1 to 14, and it was noted, as in the observations from the 4th to the 7th of September, that after the withdrawal of the starch the excess of sugar remained for several days.

Howel (see table, page 146), who excreted sugar in much greater profusion, gave results which are not dissimilar, though since circumstances interfered with the rigidity of his diet, they do not display the same regularity. The proportion of excess of urea to sugar varied from 1 to 5·4 to 1 to 11·2. The minimum proportion of sugar was reached under a diet as absolutely exclusive of sugar and starch as the composition of gluten bread permitted; the maximum under a regimen which included common bread and three pints of milk.

These statements do not refer to the last week of life, during which period the sugar rapidly fell to nothing.

In the case of Ann Mackay (see table, page 167), the ureal excess to the sugar under wheat and gluten bread was as 1 to 3·7. The successive addition to the diet of sugar, arrowroot, and then of sugar again, altered the proportion by an increase of sugar, but on the resumption of the former restricted diet, precisely the same proportion was resumed.

Looking at several cases from which details are given at page 112, we find that under restricted diet the ureal excess bore to the sugar a proportion which varied from 1 to 3·8 to 1 to 6·2, part of which variation is no doubt owing to want of uniformity of diet, and part to individual differences in the normal or habitual production of urea.

Looking at the general constancy of proportion in each case, as long as the diet remains the same, however the absolute amounts of urea and sugar may vary, we cannot but suspect that the excess of urea and the sugar are engendered by a common operation; and having regard to

the frequent repetition under a diet of meat, gluten bread, and green vegetables—a diet not absolutely devoid of starch and sugar, but as nearly so as practicable—of a ratio of 1 to about 6, we may surmise that were the food absolutely free from these substances, the proportion would not be very remote from that indicated by Haughton's theory, 1 to 5.[1]

Uric Acid.

Average of health, 55 grammes or 8 grains.

This has been stated to be sometimes absent, or to exist in traces only, or in quantities much below the normal amount. It is probable, however, that as with urea the deficiency is only apparent, the dilution of the urine rendering it difficult of estimation. In a case examined by Professor Haughton, the uric acid amounted to 4·25 grains, or about half the normal amount. The copious deposition of uric acid crystals sometimes seen in diabetes—I have seen it where the urine measured more than fourteen pints—is sufficient to show that in such instances, at least, it is in much excess, and it is probable that this is the rule rather than the exception.

A case is referred to in the table (page 113) in which the uric acid amounted to ·472 grammes; nearly the average of health.

Sulphuric Acid.

Average of health, 2 grammes.

In two mild cases, in which I estimated the daily excretion of this acid, it amounted respectively to 1·48 grammes and 1·28 grammes. In a more severe instance I found it to amount to 2·25 grammes; in another to 4·27. All these were under ordinary diet and without medicine. The healthy average of sulphuric acid is, according to

[1] For some interesting calculations relating to this subject, see a paper by Professor Haughton 'On the Phenomena of Diabetes Mellitus,' 'Dublin Quarterly Journal of Medical Science' for October 1861.

Parkes, 2·012 grammes for the twenty-four hours, so that none of the amounts specified can be considered abnormal. 4·19 grammes and 5·4 grammes have[1] however been found as the daily excretion of diabetics under a meat diet. It is known that the sulphuric acid of the urine commonly increases with the amount of animal food, and it may be partly from this cause that in severe diabetes the excretion of sulphuric acid is increased.

CHLORINE.

As in health, the amount of chlorine, discharged as it is in the shape of chloride of sodium, is very variable. As a rule it is increased; sometimes, apparently in connection with large eating, and perhaps also with inaction of the skin, the escape of chlorine or chloride of sodium with the urine is extraordinarily increased. As much as 36 grammes of the latter or 22 grammes of chlorine, nearly thrice the average of health, have been discharged in the twenty-four hours. It does not always happen, however, that the amount is above the normal; Professor Haughton found 155 grains of chlorine[2] in one instance to be the daily amount, a quantity which comes quite within the range of health; and I have elsewhere (page 112) stated the urinary chlorine in three diabetics under ordinary diet as respectively 4·43 grammes, 2·49 grammes, and 5·7, all of which are below the mean.

Average of health, 8 grammes.

PHOSPHORIC ACID.

This varies much in amount in different subjects and with the same subject in different circumstances. When the urine is superabundant, the appetite great, and the food comprises common bread, it may be in considerable

Average of health, 3 grammes.

[1] Parkes on the Urine, p. 344.

[2] 'Dublin Quarterly Journal of Medical Science,' November 1861, p. 268.

excess of the normal amount, as in a case referred to at page 113, where as much as 5·1 grammes were excreted. And taking other similar cases, it often appears that at times the phosphoric acid is in some excess, though only so long as the appetite remains voracious, and the food be of a kind to supply the material. In the case of the boy Howel (page 146) the phosphoric acid was often above his due, once over 4 grammes. It however varied greatly; during a month in which he had bran cakes, it was always short of 1 gramme. With gluten bread together with a little common bread, it was more abundant, and reached 3 grammes within a few days of his death. Finally, however, with the cessation of glycosuria and the failure of appetite, it fell almost to nothing.

The woman Mackay (page 167), under common bread, passed 4·5 and 3·2 grammes. The amount fell on the approach of death. Professor Haughton found more than 13 grammes in a case he relates in the paper which has been already referred to.

There are numerous instances, however, in which the excretion of this acid has not much varied from the normal standard, and others in which it has been reduced. In the case of Kirby (page 161), it scarcely reached the usual level at any time, and finally with the failure of appetite, was much below this. In the table (page 112) are several examples in which the excretion of this substance was abnormally low, in one only ·65 grammes.

There are reasons which suggest that while the larger part of this acid, that which is combined with the alkalies, varies with the quantity and character of the food, the smaller part, that which is associated with the earths, may be specifically increased by the disease. Further particulars will be found in the next paragraph.

Lime and Magnesia.

Healthy average of lime ·26 grammes;

In some cases of diabetes there is a remarkable increase of lime; in others this earth does not exceed its normal amount.

In the case of Mackay (page 170 and 171), the lime, on three estimations, amounted respectively to 2·76 grammes, 3·19 grammes, and 3·38 grammes, the smallest of these being at least ten times the average of health. The magnesia was also increased, but by no means proportionately; it reached ·52 grammes, or about twice its normal quantity. There was nothing in the food, drink, or medicine to account for any increase in the excretion of lime. The patient being in the hospital, ate and drank precisely as other diabetics who displayed no such excess. Neither had the exit of lime any constant relation to that of sugar, as one could not but think possible, seeing the affinity between the two substances. Less lime was discharged, while the excretion of sugar was artificially increased by the addition of that substance to the food than later in the disease, when the glycogenesis had been reduced by withdrawal of that item of diet.

of magnesia ·20 grammes.

In the presence of many facts which show a connection between the elimination of lime and the state of the nervous system, I am disposed to attribute the enormous escape of this earth in the present case to the extent and activity of the changes going on in the brain and cord.

Captain H. (page 113), who had the disease also in a severe form, passed in one day 2·27 grammes of lime, ·33 of magnesia; an excess of the former nearly as great as in the preceding instance. Mr. D—— (table, page 113) passed ·98 of lime and ·44 of magnesia. Joseph Howel (page 174) passed ·962 of lime, ·243 of magnesia. Ann Nicholls, a hospital patient, passed ·774 of lime, ·143 of magnesia. Both these patients were dieted diabetically upon meat and gluten bread, and drank the water of the hospital well, which is exceptionally soft. Kirby (page 160), under the same external influences, passed lime which, except when he took lime water experimentally, rarely exceeded the limits of health; on one occasion it reached ·526, the corresponding magnesia being only ·096.

Other examples are to be seen in the table (page 112), where the lime being between ·3 and ·5 grammes reached

the highest range of healthy production; and there are others, mostly slight and chronic cases, in which it is not above the healthy average.

Reference to the cases which have been adduced will show that there is a general correspondence between the variations of lime and of phosphoric acid. It is obvious that since the lime appears in the urine as phosphate, its admission in excess into that secretion must be attended with a corresponding addition to its total of phosphoric acid; and a reference to the quantities will show that the augmentation of acid is about as much as can be thus accounted for.

Exceptional instances may be adduced in which the earth and the acid have not varied together; with Kirby (page 161), when his end was approaching and his appetite gone, the phosphoric acid lessened, but not the lime. With abstinence, one source of phosphoric acid was cut off. The lime still continued to pass with almost exactly as much of the acid as was required for its conversion into phosphate. It would seem that this compound was obtained from the body, not from the food.

There is a relation evident enough clinically, however obscure in its mode of production, between irritation, mental or morbid, of the nervous centres, and the excretion of lime. The only explanation which suggests itself is this. The brain abounds in phosphorus, though containing less lime than almost any part of the body. Waste of cerebral or nervous tissue may discharge phosphoric acid in superabundance into the blood. This may act as the solvent of lime that would otherwise remain in a solid state, and cause its premature discharge in the urine.

For further particulars on this head I must refer to a subsequent chapter, where will be found other observations which relate to the connection, more easy to exemplify than explain, between nervous perturbation and the excretion of phosphate of lime.

Alkaline Salts.

It has already been stated that in diabetes the chloride of sodium is greatly increased, and probable that from their necessarily increased admission with food there is some increase in the other salts. The instances at page 112 do not show any marked increase in the sum of these substances, and it is probable that any increase they undergo must be considered accidental rather than essential.

Average of health about 16 grammes—much variation.

CHAPTER VI.

TREATMENT.

The treatment of diabetes may be divided into two parts—dietetic and medicinal—the first essential, the second accessory.

The regulation of the food is of paramount importance, insomuch that were the disease treated by this means only, it may be doubted whether its subjects would not on the whole be gainers. The first law is to give what the diabetic system can keep as food, and withhold what it expels as sugar.

Necessity for restriction of diet.

The expulsion of food as sugar involves the inanition—loss of substance and temperature—attendant upon its loss; it also, from the water which it carries out with it, causes dehydration with consequent thirst, constipation, and general glandular inactivity. And the excess of sugar is injurious in its accumulation as well as in its exit. In the blood it is detrimental to the tissues and dangerous to life. It causes cataract. It has been thought to cause the pulmonary destruction belonging to the complaint, though, as will be seen elsewhere, another origin for this lesion may be suggested. And it is apparently chiefly concerned in the production of the coma which so often concludes the disease. Sugar, and what in diabetes is transformed into sugar, must therefore be withdrawn from the food. The credit of this device is due to Dr. John Rollo,[1] an army surgeon, who wrote at the end of the last century.

Sugar and starch.

In severe forms of the disease sugar and starch pass through the body apparently unused; they enter the urine with the least possible modification, and contribute nothing to heat or nutrition.

Protein bodies.

Protein bodies in

[1] Notes of a Diabetic Case. 1796.

Gelatine, fat, and alcohol.

the same circumstances, albumen, fibrin, and casein, are in part rendered useless by immediate transformation, as we must suppose, into sugar and urea, but a proportion remains subservient to the purposes of the body. Gelatine, fat, and alcohol are thought entirely to elude the destructive efforts of the disease, and to be assimilated or applied as in health. When the disorder is less severe the powers of appropriation are greater.

In a well-marked class of cases, sugar ceases from the urine when together with starch it is withdrawn from the food. But the extremities of the diabetic series, widely as they may differ in some respects, must be treated on the same principle, the practical issue of which is to abstract from the food whatever increases the discharge of sugar with the urine, never pushing restriction to obvious injury of the general health.

In a severe case the exclusion of sugar and starch may be as nearly absolute as possible; when the disease is mitigated, so may be the restriction.

Details of diet.

In detail a patient with thirst, diuresis, and emaciation must be debarred, among the necessaries of life, from bread, potatoes, and milk, and, among its luxuries, from sugar, fruit, and beer. He may take flesh, fish, and fowl in all their variety, and need not eschew the fat, since this hydrocarbon appears not to be amenable to saccharine perversion.

Diabetics have, with a somewhat pharisaical devotion to the letter of the law, been bidden to abstain from the liver in consequence of the sugar or glycogen it contains; an observance necessary for theoretical perfection, but scarcely of enough practical result to warrant its addition to the long code of diabetic prohibitions.

Every kind of soup and broth into which prohibited vegetable products do not enter is admissible; unsweetened jelly and eggs. Although in severe cases, milk, as such, must be avoided in consequence of the sugar it contains—no less than 3 per cent., or about half an ounce to a pint—yet since this material is confined to the whey, all the other derivatives of milk—cheese,

cream-cheese, cream and butter—may be freely used. The same may be said of curds and of what may be generally but is not always distasteful, sour milk, or butter-milk, the sugar of which has become converted into lactic acid.

In slight or early cases, however, milk can often be taken in moderation without injury; animal sugar is more easily assimilated than vegetable sugar, and in the milder forms and stages may be perfectly digested.

Substitutes for bread.

Gluten bread and gluten flour, from which by washing with hot water, much of the starch has been removed, may take the place of common bread, and of common flour in all its uses.

That gluten bread is not absolutely free from starch is sufficiently evident from the following analyses, for which we are indebted to Dr. Bence Jones. It must be stated, however, that the best English gluten bread is less amylaceous than that from Toulouse.

	Water	Starch and Dextrin	Sugar	Gluten
Ordinary bread (per cent.) . . .	36	40	1	23
Aërated bread " . . .	37	42	2	19
Gluten bread from Toulouse (per cent.)	2	16 to 44	0	82 to 54
Dried bread (per cent.) . . .	2	60	1	37

It is against gluten bread as a staple of diet that the washing necessary for the removal of the starch has also to a great extent deprived it of its soluble salts.

The ash of wheat consists chiefly of the phosphates of potash and magnesia, salts which, especially that of potash, are of primary importance in nutrition. The same objection does not apply to the bran cake.

I have appended a statement showing the amounts of alkaline and earthy salts, and the total of phosphoric acid in the common aërated bread of the hospital, Bonthron's gluten bread, and Blatchley's bran biscuit. There is no loss of the total of phosphoric acid in the medicated breads, on the contrary, especially in the bran biscuit, a

great increase. The only loss is in the soluble phosphates and in the gluten bread.

Salts and Phosphoric Acid in Common Bread, Gluten Bread, and Bran Biscuit.

	In 100 parts as used			In 100 parts dry		
	Alkaline salts	Earthy Salts	Phosphoric Acid	Alkaline Salts	Earthy Salts	Phosphoric Acid
Common aërated bread	·792	·397	·272	1·243	·618	·427
Gluten bread . .	·214	·648	·334	·307	·930	·479
Bran biscuit . .	1·105	3·630	1·72	1·184	3·904	1·81

N.B.—The alkaline salts may be taken, consistently with the known composition of the ash of wheat, as composed chiefly of phosphate of potash; the earthy salts as chiefly phosphate of magnesia.

Fresh meat, green vegetables, and a proportion of bran biscuit may make up the deficiency; but if a further correction be needed, it can be afforded by the syrup of the mixed phosphates known as Parrishes' chemical food; or by adding phosphate of potash to the habitual tonic, this salt being often additionally useful by reason of its slight aperient effect.

Next to gluten bread, bran cakes are to be recommended: bran freed by careful washing from adhering starch, ground to flour and made into cakes, supplies a food almost as non-amylaceous as gluten bread. They are too hard and dry to be palatable, but are useful as counteracting the constipation which is one of the troubles of the disease. Bran is useful as affording variety, though gluten may be the best staple. A further change is to be found in Pavy's almond biscuits which, however, are rather a luxurious addition to diabetic fare than adapted to take the place of daily bread. In the almond oil takes the place of starch and exists in the fruit in the proportion of 54 per cent.; except therefore a small admixture of sugar, the almond and all fruits of similar composition, hazel nuts, walnuts, and cocoanuts, are unobjectionable.

Greens. 'Greens' as the phrase is, or boiled green leaves, are important items in the bill of fare. The green colouring matter is made by the sun at the expense of the sugar and starch, and the absence of these substances is further ensured by the action of hot water. White vegetables, on the contrary, celery and sea-kale, and all roots, should be avoided.

Drinks. Drinks may be classed as especially injurious in simple proportion to the sugar they contain. The patient may choose among the products of the still, careful only to avoid those like gin and liqueurs which have been subsequently sweetened. He may take claret and Burgundy, of the latter the white sorts, Chablis and Grave, as well as the red. He may choose among the vineyards of the Rhine and the Moselle, careful only to avoid effervescent wines, which from imperfect fermentation and saccharine additions are objectionable. These excepted—and the prohibition equally applies to champagne—the wines which have been mentioned are nearly or quite devoid of sugar. He must shun port, madeira, all sherry but the driest, cider and all malt liquors save the pale bitter ale made by Bass and Allsopp for the Indian market, which is fermented fully in making and further in bottle. Bence Jones found an ounce of bitter ale to contain from 12 to 130 grains of sugar; Pavy in the same quantity of bottled Bass found little more than 2 grains. Bitter ale, therefore, varies greatly, and must be selected with caution, but with its minimum of sugar it is often useful in consequence of its nutritious and appetizing properties.

Bavarian beer would probably be the best were it readily obtainable.

There is no reason to suppose that alcohol has especial use in diabetes, though sometimes, as with diuresis from other causes, remarkably tolerated. I saw this once in the case of a stout French gentleman who preserved his sobriety under a daily potation of 20 bottles of claret besides beer and one bottle of brandy.[1]

[1] For this statement I have as much evidence as is possible short of having

Strict Diabetic Diet.

What to Eat	What to Drink	What to Avoid
Fresh meat abundantly, without exclusion Meat, salted, smoked, cured, potted, or preserved in any way excepting with honey or sugar Poultry and game of every kind Fish of every kind, fresh and preserved Soup of all kinds made without common flour or prohibited vegetables. Unsweetened jelly Isinglass Oil, dripping, and suet Butter Cheese Cream cheese Cream Curds Cooked green vegetables, cabbage, cauliflower, spinach, broccoli, Brussels sprouts, turnip tops, French beans, the green ends of asparagus Uncooked green herbs, lettuce, water-cresses, mustard and cress Gluten flour and bread Bran flour and cakes Almond flour and cakes Almonds Nuts and filberts Walnuts Brazil nuts Cocoa nuts Condiments Glycerine	Water Soda, seltzer, and all mineral waters Tea, coffee, and cocoa from the nibs All unsweetened spirits, cognac, whisky, Dutch hollands, unsweetened gin, rum Claret Red burgundy White burgundy, chablis and grave Hock and still moselle The driest pale sherry Amontillado or Vino de Pasto	Sugar and treacle Honey Common flour Bread Macaroni and vermicelli Corn flour Arrowroot Sago Tapioca Oatmeal Barley meal Potatoes Beetroot, parsnips, carrots, turnips, radishes, onions, and all roots Celery, seakale, and rhubarb Peas and beans Chestnuts All sweet and preserved fruits Milk Whey Skimmed milk Chocolate All malt liquors with the specified exceptions Cider Champagne and all sparkling wines Port, madeira, and all sweet wines Sherry except the driest Sweetened spirits Liqueurs

Modified Diabetic Diet.

Add toasted bread ,, celery and seakale	Add bitter ale ,, milk	

witnessed the feat. The patient himself admitted that such had been his habit. His medical attendant, a gentleman of character and position, who had watched him closely, corroborated the assertion and bore witness to the daily relays of empty bottles; and the innkeeper—the gentleman lived at an hotel—testified to the consumption, and to the pecuniary loss to himself, when, under medical pressure, the daily number of bottles was stinted to six.

Where there is much production of sugar and concomitant wasting, and the appetite is not below par, which it seldom is until the end is approaching, this regimen may be kept to. It should not be begun suddenly nor pursued with too unvarying a course.

The amelioration is usually obvious and not long delayed. The thirst lessens, the parched mouth becomes moist, the spirits become more elastic, bulk and strength increase, and virility, which seemed permanently lost, has, in some instances, been recovered. Thus rejuvenant, the patient may cheerfully submit to the small restrictions to which he owes so much. And looking at the variety of the materials permitted, and at the extent to which this variety can be magnified by the permutations and combinations of ingenious cookery, he must be hard to please who cannot both stay his stomach and sufficiently gratify his palate upon his bill of fare.

That such a diet is more than enough for health is evident in the subsistence of many races upon one much more narrowly restricted. Dried flesh, or pemmican, which is a cake made only of meat and fat, suffices to keep the Red Indian or European trapper in full vigour for unlimited periods.

Relaxation of rules sometimes necessary or advisable.

If the patient has retained, or under treatment acquired, the larger powers of assimilation which belong to the milder form or earlier stage of the disease; or if failing nutrition show him to be intolerant of restriction; the dietary may, with little departure from its principle, be supplemented with highly toasted or nearly charred bread, much of the starch of which has been thus disorganised. Milk may be superadded, animal being less objectionable than vegetable sugar; celery and seakale may be added to the list ot cooked vegetables, and the prohibition may be removed from the less saccharine beers.

With the failure of appetite it may be necessary to abolish all restrictions.

In treating diabetes dietetically it must ever be borne in mind that the chief danger lies in inanition. It is

more important that the food should be sufficient than that it should be wholly non-saccharine. When, therefore, appetite or digestion rebel against the specified regimen, mixed food is better than none.

Treatment by sugar.

After what has been said, it is scarcely necessary to allude to the treatment of diabetes by sugar suggested by Piorry, in the belief that its discharge, instead of being the result of an injurious excess, was the cause of an injurious deficiency. The disorder in this view is not of increased production, but only of increased excretion; a mistaken view which is sufficiently refuted by the superabundance of sugar in the blood, the tissues, and the secretions. Within the body sugar is not wanting, but is in harmful excess; and sugar from without can only give its sum of more to that which has too much.

By the test of experiment it has been placed beyond doubt that sugar in diabetes is worse than useless. The discharge by the urine is, in a well-marked case of the disease, increased by about the amount of the sugar ingested, and the diuresis, thirst, and the general discomforts of the disease are correspondingly exasperated.

Skim milk.

Similar reasons militate against the use of skim milk, a remedy which would seem to be something of a panacea, since its virtues embrace not only diabetes, but also granular degeneration of the kidney and Addison's disease of the supra-renal capsules. For diabetes this preparation of milk would seem to be doubly unsuited, for it is deprived of the cream which might in moderation be useful, and it contains the sugar which in all but the mildest cases is injurious. If Dr. Donkin be right, much false observation has held its place from the dietetics of Rollo to the pathology of to-day:

> I care not for carping; but this I can tell,
> We preach very sadly, if he preaches well.

If the disease be in the exceptionally mild form, which allows of the assimilation of milk-sugar, and the patient be corpulent and plethoric, suggesting hepatic rather than nervous glycosuria, it is not impossible that a course of starvation by skim milk, or otherwise, might be salutary.

But where diabetes occurs in a severe form and as a wasting disease, restriction to this liquid has been, as it necessarily must be, followed by the worst results. Dr. Roberts thus records what has come under his notice: 'Three chronic cases I know of, in which the treatment was obstinately persevered with, died from exhaustion.'

Of two diabetic women thus treated in St. George's, one died on the second day, possibly partly from the effects of the journey to the hospital; the other slowly sank under the process, and owed her death in all probability to it. With this experience I have myself forborne the practice.

Drink to be unlimited.

The patient may drink water as his inclination directs, and thus do his best to obviate dehydration and facilitate the escape of the sugar. The victims of diabetes, as of cholera, have, with an almost religious distrust of the promptings of nature, been stinted of water apparently for no better reason than because they suffer from thirst. The thirst, however, in both cases, indicates that the blood contains less than its due proportion of water, and should be satiated as indicating a need rather than discouraged as an injurious propensity.

The patient may drink water acidulated with phosphoric acid, or with acid tartrate of potash; or may take ordinary lemonade, sweetened with glycerine instead of sugar.

Diabetic persons require free exercise in the open air, as far as may be. They profit much by change, and do better as a rule in the country than in London. They need especially warm clothing as a means of obviating the low bodily temperature which is one of the results of the disorder.

Drugs of secondary importance.

Next as to drugs. In the probable first stage of diabetes, dilatation of the cerebral vessels, it is conceivable that the disorder may be within the control of therapeutics, and to this end I have made many trials with remedies which act upon the brain and nervous system, hoping to light upon one which should tell upon the glycogenesis directly and at its source.

But such an antidote even to early glycosuria, unless it exist in opium, which at best is uncertain and unsafe, has yet to be found; and it needs no failures to teach that the extensive cerebral lesions of the advanced disease are beyond the *ars medendi.* Drugs, therefore, must be directed to palliation rather than cure, though even in the relief of symptoms, to which they must be restricted, they occupy a place second in importance to diet. It is not to be supposed, however, that drugs are useless. The therapeutical scheme may comprise tonics and restoratives habitually, with special remedies to meet especial symptoms.

Strychnia is of the first importance, and liver oil perhaps of the second. Iron is often of use, as also are the mineral acids, especially the phosphoric.

Strychnia.

Strychnia is of all medicines the most constantly useful; it restores and preserves the general health, in a manner equally welcome to the patient and evident to the physician. The improvement upon replacing opium or other narcotics by strychnia is often striking. I have never been able to trace to this agent any diminution of sugar, and therefore presume that it has no specific action upon the disease, but it antagonises, in a manner not to be mistaken, its lowering effect. The liquor may be begun in doses of 3 or 4 minims, increased up to 10 or 12, and continued for an indefinite period. I have given harmlessly, if not beneficially, doses more than twice as large as the largest of these.

Cod-liver oil.

Cod-liver oil, which like other oils resists saccharine perversion, has value as food rather than physic. It maintains the strength and retards emaciation. Though not a remedy for the disease, it is a direct remedy for some of its effects, and where there is much tendency to emaciation is productive of marked benefit.

Iron.

Iron is especially useful as a means of counteracting the poverty of blood which the disease engenders. It is the one remedy for diabetic œdema. It is sufficiently striking to see fluid collect in the limbs while perhaps 16 pints a day are escaping by the kidneys. Such dropsy

is not for want of diuresis. On the contrary its origin is anæmic, and its cure not by withdrawal, but replenishment. Perchloride of iron is almost antidotal, the action of the medicine being as noteworthy as the access of the symptom. The tincture may be given three or four times a day, in doses of from 20 to 40 minims.

Other tonics.

Other medicines of the tonic class are occasionally useful; arsenic, the products of the cinchona, and other vegetable bitters. As a rule, however, none do as much good as strychnia.

Purgatives.

It is essential that inactivity of the bowels should be obviated. The patient never fails to suffer if allowed to go long without relief. The diabetic smell increases, and there may even be risk of diabetic coma. Bran, in cakes or flour, will do something; castor-oil, the vegetable aperients, and an occasional dose of calomel, will do the rest. Salines are best avoided, as they are apt to prove diuretic.

Mineral acids.

Of the mineral acids the phosphoric is the most serviceable: it allays thirst, it has a laxative effect which is often a desideratum, and it may possibly act usefully in supplying a deficiency in the gluten bread. Neither this, however, nor any other mineral acid, affects the production of sugar. I have given six drachms of the dilute phosphoric acid with two drachms of phosphate of ammonia daily without result.

With animals the injection of phosphoric acid into the veins far from preventing, causes, glycosuria.[1]

Alkalies.

Passing from acids to alkalies,[2] Dr. Pavy found that the injection of carbonate of soda into the jugular vein prevented the appearance of sugar in the urine when subsequently the upper cervical ganglion was removed, and inferred that the alkali inhibited the glycosuria by a change it produced in the blood.

This lends support to the old view, according to which alkalies were remedial as promoting oxidation, the de-

[1] Pavy on Diabetes. 2nd edit. p. 176.
[2] Loc. cit.

ficiency of which was the essence of the disease. If, however, the disorder depends, as I think must be admitted, not on any deficiency in the supply of oxygen, but on an exaggeration of hepatic function from nervous influence, it becomes not so much a question of material as of arrangement, and to attempt to cure by oxidation is to aim beside the mark.

The oxidation theory, however, has led to the extensive use of alkalies in diabetes with a belief in their specific action. They have been given by the mouth, injected into the bowels, and the alkaline waters of Vichy, Vals, Carlsbad, and Marienbad have been used as habitual drinks. It is certain that alkalies have no especial or curative action. I have given for long periods large doses of carbonate and citrate of potash certainly without beneficial result, and I find that the experience of Dr. Roberts coincides with my own. In the mild glycosuria which is sometimes associated with plethora and uric acid, alkalies may, on general principles, be of use. If mineral waters are used, those are best which, like Carlsbad and Marienbad, are aperient from the sulphate of soda they contain.

Peroxide of hydrogen, in watery solution, or as ozonic ether, has, on the same oxidation theory, been advanced as an antidote for diabetes. As far as any effect upon the disease is concerned I have found it to be absolutely inert. And the amount of oxygen to be introduced by such means is not such as, on any view, to promise great results. Mr. Robbins, by whom chiefly the peroxide is prepared, tells me that the solution is capable of yielding ten volumes of oxygen. Thus supposing the unusual amount of one ounce to be swallowed in the day, about 20 cubic inches of oxygen would be put into the stomach. Presuming all this to enter the blood in an active state, that fluid would receive by such means less than one thousandth the amount of oxygen it obtains through the lungs in the same space of time—an aspect which causes peroxide of hydrogen as a remedy for diabetes to degenerate from a fallacy into an absurdity.

Peroxide of hydrogen.

Opium.

Opium is the only drug which can be credited with any curative action in diabetes; and its power in this respect is so limited that it may well be believed to have cured fewer of the subjects of the disease than it has killed.

Pelham Warren,[1] in the year 1812, I believe first proposed opium as a remedy for diabetes. He gave as much as 20 grains a day, and found that they, in conjunction with animal diet, mitigated the general symptoms and caused the urine to lose its superabundance and its sweet taste. Opium has since been very generally used in the treatment of the disorder. It reduces, I think invariably, the excretion of sugar and in exceptionally mild cases has been known to arrest it altogether. In its power of diminishing nervous sensibility it would seem fitted, according to our present knowledge, to allay the glycosuric irritation at its source, and so act directly in the cure of the disease.

Whether it does so is still *sub judice*. The lessened excretion of sugar under its influence is not all for good. The appetite is impaired, and so less of the saccharine element is introduced, possibly to the injury of the patient. And the glandular activity of the kidneys is lessened, whereby the sugar escapes with less freedom and may accumulate. Glycosuria in animals may be produced by morphia. Whether from saccharine accumulation or not, it needs no large familiarity with the disease to show that the use of opium in diabetes is not without danger. Under its influence the bowels are apt to be obstinately confined, the tongue to become thickly coated, dyspepsia and epigastric pains to occur, and too often a lapse into that coma which sometimes suddenly abridges the course of diabetes. I believe that the risk of this premature ending is greatly enhanced by the indiscriminate use of opium. The lesions of advanced diabetes are such as no opium can

[1] Two Cases of Diabetes Mellitus treated with Opium. 'Medical Transactions of the College of Physicians' vol. iv. p. 188.

cure; and as a matter of experience at this stage of the disorder, this sedative, though it never fails to lessen the discharge of sugar, is absolutely impotent as arresting the course of the disease.

When the complaint is incipient or slight, opium may help to cure. The sugar, as Dr. Pavy recommends, should first be reduced as far as possible by diet; opium then used in moderate or cautiously increased doses, and with a watchful care against constipation, will reduce the sugar further, without risk to the patient, and within the limits of possibility banish it altogether from the urine. I found it convenient to prescribe the opium together with a countervailing dose of compound colocynth, half a grain or a grain of the narcotic with two or three grains of the aperient, twice or thrice daily.

Among the alkaloids of opium codeia, as that to which the antiglycosuric action is chiefly attributed, has been thought to do the good of opium with a minimum of harm. Dr. Pavy is the great advocate of this drug; he gives it, as he tells me, in almost every case, in doses slowly increased from a quarter of a grain to two grains, three times a day; and believes that it not only lessens the excretion of sugar, but exerts a restorative influence upon the morbid condition which produces that discharge. That like opium it lessens, and sometimes suspends, the excretion of sugar is certain; while at the same time it controls the symptoms which immediately depend upon the loss; but it would seem that cures so wrought are not permanent, nor is the fatal issue averted by its action.[1] Codeia.

I have searched among other sedatives and narcotics for one which should have the use of opium without its disadvantages, but I have not succeeded in finding any other which exerts a beneficial influence upon the course of the

[1] For illustrations of the kind and amount of good to be expected from codeia, see cases published by Dr. Pavy, in the 'Guy's Hospital Reports' for 1869–70.

disease or even decidedly controls the excretion of sugar. There is marked tolerance of at least the vegetable narcotics.

Belladonna. I have given belladonna to the extent of dilating the pupils and causing a pseudo-scarlatinal rash without any diminution in the quantity or specific gravity of the urine. Kirby, whose case is related at page 157, took, with a negative result, no less than 15 grains a day of the extract.

Cannabis Indica. Cannabis Indica can be given in diabetes with a remarkable absence of result. In the case of Mackay (page 167), 20 grains of the most trustworthy extract were given daily with no further consequences than some drowsiness and flushing of the face. A reference to the case will show that rather more sugar was passed after the course of cannabis Indica than at its commencement under the same diet. I gave to another diabetic patient doses of the extract gradually increased up to 42 grains a day with no result save slight frontal headache, drowsiness, and giddiness. The sugar under this amounted to 238 grammes, the previous range under the same diet having been from 228 grammes to 292. Thus Indian hemp, though singularly tolerated, has no special effect upon diabetes.

Calabar bean has been tried and found useless.

Chloral. I have frequently given chloral and always with a negative result.

In the case of a man 24 years of age who had had diabetes for six months, I alternately gave and withheld chloral. It was given every four hours in doses of from 10 to 15 grains. The same diet, which was unrestricted, was continued throughout. In the averages I have left out fractions.

Without medicine for 8 days, gained 6 lbs. in weight. Average quantity of urine 104½ ounces; average sp. gr. 1,032.

Under chloral for next 22 days, gained 3½ lbs. weight. Average quantity of urine 82 ounces; average sp. gr. 1,034.

Without medicine for next 14 days, weight of body remained

constant within half a pound. Quantity of urine averaged 69 ounces; sp. gr. 1,036.

Under chloral for next 4 days, the quantity of urine averaged 71 ounces, the sp. gr. 1,034.

Thus large doses of chloral had no discernible effect upon the quantity and specific gravity of the urine. A diminution at first observed in its quantity was probably due to causes other than the chloral, since it still further diminished when this agent was withdrawn.

Without the chloral the pupils were dilated, and the ophthalmoscope, which Mr. Carter was kind enough to apply, showed great dilatation of the retinal veins. Under the chloral the pupils became less dilated and the dilatation of the retinal veins ceased.

Under the chloral the appetite remained good, and the pulse natural. The patient looked flushed and turgid, and was generally found to be dosing in a sort of after-dinner stupor. He walked about with a congested look and drowsy manner as if half asleep. He had no headache.

Shortly after these observations the patient died of the diabetic caseation and excavation of the lung, which ran its course with extraordinary rapidity.

Bromide of potassium in full and frequent doses has in my hands proved as ineffective as chloral in controlling the special symptoms of diabetes. Bromide of potassium.

Iodide of potassium on the other hand has an action which is not less than remarkable upon the excretion of sugar, though there is no reason to suppose that it is a remedy for diabetes. The effect of this salt in certain other chronic diseases of the nervous centres led me to use it experimentally in this. Iodide of potassium.

In the case of Kirby (page 160) is recorded a striking diminution of sugar and urea under this agent, but the experiment was complicated by the addition of a little laudanum required to check diarrhœa.

Joseph Howel (page 178) passed 292 grammes of sugar. The iodide at a minimum dose of 30 grains a day, reduced it to 51 grammes. The sugar recovered nearly its former

abundance on the discontinuance of the drug. A repetition of the iodide from 60 to 40 grains daily, reduced the sugar from 238 grammes to 110 grammes; the urea at the same time falling from 59 grammes to 34 grammes. Where the diabetic sugar has been reduced to this extent by iodide of potassium, it has been at the expense of much prostration, insomuch that it must be questioned how far the diminished excretion is due to loss of appetite. A woman 34 years old was kept upon an unvarying restricted diet. On February 21, she passed 200 grammes of sugar and 32 of urea. Ten grains of iodide of potassium were given every six hours. On March 21, she passed 137 grammes of sugar. There was no loss of appetite. The patient had lost weight to the extent of 2½ lbs. She looked less hearty but was not definitely weakened or ill. Continuing the iodide the sugar increased again, amounting on April 25 to 197 grammes, the urea at the same time to 34 grammes. The iodide now being withdrawn, the sugar on May 23 was found to amount to 196 grammes, the urea to 41 grammes.

In this instance, therefore, the salt which had little effect upon the appetite scarcely affected the excretion of sugar or urea. In other cases, where the appetite has suffered, both these constituents of the urine have lessened proportionately. It may therefore be presumed that the remarkable diminution of sugar which sometimes occurs in diabetes under this salt, is not the result of any mitigation of the disease, but of loss of appetite and general depression of function. I have never found the saccharine diminution thus caused to be permanent, nor been able to trace to it any amelioration in the general condition of the patient.

It has been noticed that a disease with many remedies is generally little under the influence of any. And diabetes has many cures which it would be no less unprofitable than tedious to trace from their origin in speculation to their extinction in practice.

Rennet has been given with the ingenious notion of converting the sugar formed in the body into lactic acid. Probably, even if it did so, the subjects would not materially profit since the evil lies not so much in the presence of the sugar as in the loss of the food which is thus converted. Dr. James Gray[1] considered seven of twenty-eight diabetics treated by this agent, together with restriction of diet, to have been cured by its means, but the practice has failed in other hands. And lactic acid[2] itself has been thought to be remedial on the ground that by its ready conversion into carbonic acid and water, it would increase the organic combustion supposed by its advocate to be deficient. I have given lactic acid in several cases and failed to observe any ensuing benefit. Pepsine has been commended, but, as with many other supposed remedies, there is a lack of concurrent testimony in its favour. Dr. Bence Jones found that under its use the sugar did not diminish, Parkes that it increased.

Rennet.

Lactic acid.

Galvanism, and what are termed electric baths, have been used in diabetes, but we have no such evidence of their utility as to entitle them to our consideration.

Galvanism.

To sum up, it is usually of paramount importance to reduce the production of sugar by diet, the degree of restriction varying with the nature of the case.

Summary.

Medicinally an early and mild case, one in which it is possible that the vascular disturbance may not have proceeded to extensive injury or destruction of tissue, may sometimes be beneficially treated by opium or codeia; but with such exceptions, and they are few, these drugs fail to check the course of the disease, however they may modify its leading symptom, and are but too often injurious.

In severe and advanced cases, where the nature

[1] 'Dr. James Gray on Diabetes Mellitus.' 'Glasgow Medical Journal,' 1857, page 252. 'Roberts on Urinary and Renal Diseases,' 2nd edit. page 255.

[2] 'British Medical Journal,' Feb. 25, 1871. Account of Professor Cantani's researches on Diabetes.

of the cerebral lesions and the observed intractability of the disease are alike discouraging, we can but contravene the symptoms—the inanition, the nervous and general depression, and the inactivity of the bowels. Strychnia, cod-liver oil, and iron are the drugs to which the highest value must be attached, as directed towards this end.

CHAPTER VII.

CASES IN ILLUSTRATION OF THE SYMPTOMS, PATHOLOGY, AND TREATMENT OF DIABETES MELLITUS.

THE following cases exemplify some of the points of pathology, symptoms, and treatment to which reference has been made.

CASE 1.

Diabetes fatal by excavating pneumonia. Weekly record of sugar, urea, phosphoric acid, body-weight, and temperature. Effects of belladonna, arsenic, opium, iron, strychnia, and lactic acid. Final disappearance of sugar from urine, and death from exhaustion.

James Howel, 18 years of age, suffering with diabetes, was sent from Cold Norton to be under my care at St. George's on October 28, 1870.

Three years later his father, who had been attacked since his son's death, became my patient in the same place.

The son had been for two years assistant to a grocer, where, as he thought, the complaint was produced by over work, particularly in respect of lifting heavy weights and carrying them up ladders, such efforts being often succeeded by pain in the forehead.

When new to his employment he ate sugar and plums to excess, but not afterwards. He had had no trouble, anxiety, or privation. The hereditary tendency not having as yet declared itself in the person of the father, it was surmised that the disorder might have arisen in strain, with over distention of the cerebral vessels and minute hæmorrhage by migration.

Eighteen months before admission the symptoms began with thirst and parching of the mouth, succeeded almost immediately

by much increase of urine, and gradually by loss of flesh and failure of strength. Two months after the thirst became troublesome he noticed increase of appetite, which he indulged at the expense of a quartern loaf a day, getting meat but seldom. In the February of 1869, increasing weakness compelled him to leave his situation and the disease was detected. Latterly his memory had failed, the events of the war in progress between France and Germany, in which he had been much interested, leaving his mind totally and permanently.

October 28, 1870. He was a weakly-looking under-sized boy with pale complexion and light brown hair. His limbs were attenuated: the skin harsh and branny, the tongue red, the pulse weak, 104. He weighed 7st. 1lb.

The progress of the case and the results of treatment may be briefly displayed in a tabular form.

Date	Treatment	Urine							Body Weight	Temperature		Progress
		Quantity (C. C.)	Specific Gravity	Sugar	Urea	Proportion of total Urea to Sugar 1 to —	Proportion of excess of Urea to sugar allowing 3 grammes to a stone 1 to —	PO_5		A.M.	P.M.	
				grms.	grms.	grms.	grms.	grms.	st. lbs.	deg.	deg.	
1870 Oct. 31	Extra meat, 4 eggs, 2 pints of beef-tea, 3 pints of milk, greens, toasted bread.	12950	1028·6	917	142	6·4	7·6	3·23	7 5½	—	—	Ophthalmoscopic observation (Mr. B. Carter). Turgescence of central veins of both retinæ, especially of branch proceeding downwards in left eye.
Nov. 5	—	—	—	—	—	—	—	—	—	97·5	98·0	—
7	—	9239	1030·5	608	121	5·0	6·1	3·74	—	97·6	97·6	—
8	Ext. belladonnæ gr. ¼ 4tis horis	—	—	—	—	—	—	—	—	—	—	—
12	Ext. belladonnæ gr. ⅓ 4tis horis	—	—	—	—	—	—	—	—	—	—	—
13	Ext. belladonnæ gr. ½ 4tis horis	—	—	—	—	—	—	—	—	—	—	—
14	—	10224	1032·2	715	112	6·3	7·9	4·08	7 2¼	97·7	97·7	Pupils slightly dilated. Hands very dry and branny. Feels much better.
18	Ext. belladonnæ gr. j. 4tis horis	—	—	—	—	—	—	—	—	—	—	—

Date	Treatment	Urine							Body Weight	Temperature		Progress
		Quantity (C. C.)	Specific Gravity	Sugar	Urea	Proportion of total Urea to Sugar 1 to —	Proportion of excess of Urea to Sugar allowing 3 grammes to a stone 1 to —	PO_5		A.M.	P.M.	
				grms.	grms.	grms.	grms.	grms.	st. lbs.			
1870 Nov. 21	Belladonna discontinued. Liquor arsenicalis ♏ iv. t. d.	8520	1032·4	608	85	7·1	9·6	2·55	7 2½	97·8	97·6	No material change under belladonna; bowels act daily, but motions hard. Throat more dry than formerly. Tongue dry and parched, not coated. Pulse weak, 96–100. Pupils slightly dilated. Ophthalmoscope showed no change in condition of venous congestion found before belladonna begun.
22	Liq. arsenicalis ♏ vj.	—	—	—	—	—	—	—	—	—	—	—
24	" " ♏ vij.	—	—	—	—	—	—	—	—	—	—	—
26	" " ♏ viij.	—	—	—	—	—	—	—	—	—	—	—
28	Adde med. Tc. opii. ♏ xv.	9088	1034·6	648	90	7·2	9·5	2·72	7 4¼	98·2	98·4	Looks and feels better, brighter and stronger. Legs slightly swollen last night.
Dec. 3	Ht. sennæ p. r. n.	—	—	—	—	—	—	—	—	—	—	Feet and ankles considerably swollen with soft œdema.

5	—	6120	1036·7	437	61	7·1	11·2	2·4	7 7½	98·4	98·2	—
6	Liq. Arsenici Hydrochlor. ♏ viij. Tc. Ferri Perchl. ♏ xv. Tc. Opii ♏ xv. t. d.	—	—	—	—	—	—	—	—	—	—	Slight cough, breath short when he lies down. Much œdema of legs. Appetite failing, bowels regular, pulse weak, 112. Tongue clean and moist.
12	—	8050	1034·0	536	80	6·7	9·2	1·6	7 3½	98·5	98·2	Large deposit of uric acid crystals under microscope. Œdema nearly gone, its diminution coinciding with commencement of iron.
15	Liq. Arsenicalis ♏ viij., Ferri Amm. Citr. gr. viij., Tc. Opii ♏ xv. t. d.	—	—	—	—	—	—	—	—	—	—	The swelling has now entirely ceased, its removal under the iron rapid and striking.
19	Bread stopped, 2 loaves of gluten bread substituted, extra butter, beef-tea 3 pints, milk 2 pints.	9650	1032·4	661	86	7·6	10·3	2·4	7 5	—	—	—
24	Pil. Opii gr. 1 o. n.	—	—	—	—	—	—	—	—	—	—	Does not sleep well.
26	—	5390	1035·7	359	70	5·1	7·4	1·07	7 4½	97·2	98·2	—
30	From this date until Jan. 3 gluten bread not attainable, common bread substituted	—	—	—	—	—	—	—	—	—	—	—
1871 Jan. 2	—	7950	1034·6	530	87	6·1	8·1	1·59	7 2	98·6	98·4	Marked increase of sugar and urine under common bread.

Date	Treatment	Urine: Quantity (C. C.)	Urine: Specific Gravity	Urine: Sugar	Urine: Urea	Urine: Proportion of total Urea to Sugar 1 to —	Urine: Proportion of excess of Urea to Sugar allowing 3 grammes to a stone 1 to —	Urine: PO_5	Body Weight	Temperature: A.M.	Temperature: P.M.	Progress
1871				grms.	grms.	grms.	grms.	grms.	st. lbs,			
Jan. 3	Return to gluten bread, glycerine instead of sugar in tea	—	—	—	—	—	—	—	—	—	—	—
4	Stop milk. Diet now consists of 9 ounces of meat, 1 mutton chop, 6 eggs, 3 pints of beef-tea, greens, gluten bread and bran cakes, and glycerine. Liq. Ars. ♏ x., Tc. Opii ♏ xx.		—	—	—	—	—	—	—	—	—	Looks well, feels weak, breath short, cough on lying down. Pulse 112.
9	Gluten bread not regularly obtainable. Almond cakes and bran cakes substituted	6532	1032·8	395	91·4	4·3	5·6	1·3	7 2	98·6	98·0	—
16	—	5964	1034·9	441	65·5	6·7	10·2	·89	7 2½	98·6	96·0	—
23	Pc. Med. c. Tc. Opii ♏ xxv., Liq. Arsen. ♏ xij. t. d.	4540	1034·4	303	63	4·8	7·3	—	7 3½	98·4	98·2	—
30	—	4540	1036·3	336	54	6·2	10·5	·68	7 8	—	—	—

Feb. 6	Tc. Camph. Co. ʒj. p. r. n.	3970	1034·5	233	59 5	3·9	6·3	·99	7 6½	99·2	99·4	Much cough.
13	—	3970	1038·1	317	55·5	5·5	9·6	·59	7 6	99·2	100	—
21	Strychnia now substituted for arsenic, everything else remaining the same. Liq. Strychniæ ♏ vj. Tc. Opii ♏ xxv. Ferri Amm. Citr. gr. viij. t. d.	3970	1029·7	240	43	5·5	10·9	2·3	7 0	98·2	99·0	About the same, appetite good; takes all his food. Has had no bread since Jan. 3, taking chiefly bran cakes, gluten bread seldom attainable. Not especially thirsty. Cough better but breath short. Tongue clean.
25	Liq. Strych. ♏ viij	—	—	—	—	—	—	—	—	—	—	—
27	—	4540	1029·8	259	59	4·4	6·8	3·0	6 11	99·5	103·0	—
28	Liq. Strych. ♏ ix.	—	—	—	—	—	—	—	—	—	—	—
Mar. 4	Liq. Strych. ♏ x. Gluten bread again obtained	—	—	—	—	—	—	—	—	—	—	Feels better. No twitching or especial symptoms from strychnia. Some headache. Appetite good. Pulse 108.
6	—	3970	1028·3	220	51	4·3	7·3	2·7	6 12	98·9	100	—
8	Liq. Strych. ♏ xij.	—	—	—	—	—	—	—	—	—	—	—
11	Liq. Strych. ♏ xiv.	—	—	—	—	—	—	—	—	—	—	—
13	—	3976	1027·3	209	59	3·5	5·5	3·1	6 10	102·2	103·2	Skin hot, pulse 112. Cough troublesome. Much muco-purulent expectoration. Sounds of bronchitis all over lungs; large bubbling at apices, especially in right, where is increased voice-sound and evidence of considerable excavation.

Date	Treatment	Urine							Body Weight	Temperature		Progress
		Quantity (C.C.)	Specific Gravity	Sugar	Urea	Proportion of total Urea to Sugar 1 to —	Proportion of excess of Urea to Sugar allowing 3 grammes to a stone 1 to —	PO_5		A.M.	P.M.	
				grms.	grms.	grms.	grms.	grms.	st. lbs.			
Mar. 20	—	3692	1028·8	205	59	3·4	5·4	2·7	6 9	97·3	99·9	—
21	Strychnia experimentally discontinued. Acid. Lactic. ♏ xx. 4tis horis	—	—	—	—	—	—	—	—	—	—	Cough troublesome, pulse 124, appetite failing, expectoration abundant, muco-purulent.
22	Acid. Lactic. ʒss 4tis horis	—	—	—	—	—	—	—	—	—	—	Bowels open three times, pulse 112.
25	—	—	—	—	—	—	—	—	—	—	—	Very drowsy, generally asleep when visited. Appetite failing, much cough, expectoration very purulent. Respiration 32, pulse 116, tongue coated and moist.
27	—	3120	1031·9	195	49	3·9	6·9	2·8	6 8	102	102·4	—
28	Acid. Lactic. ♏ xl.	—	—	—	—	—	—	—	—	—	—	—
April 1	Acid. Lactic ʒ j. An ounce of cream daily, Brandy ℥ iv.	—	—	—	—	—	—	—	—	—	—	Cannot eat gluten bread, bowels act two or three times a day, less sleepy, pulse 124. Much œdema of legs, especially of left.

3	Tinct. Ferri. Perchl. ♏xxx., Liq. Arsenici Hydrochl. ♏ x. Acid Phosph. dil. ʒss., Tc. Opii. ♏ xxx. 6tis horis. Discontinue Lactic Acid.	3120	1026·3	127	49	2·6	4·4	3·1	—	101·2	103·2	Weaker, less thirst, pulse 120 very weak. Tongue dry and red.
8	From this time diet not rigidly restricted	1270	1021·1	5·5	45	—	—	—	—	—	—	Great want of appetite.
10	—	1020	1017·6	0	32	—	—	0·1	—	99·2	100·4	Abundant deposit of pale lithates in urine with uric acid crystals.
11	Died.	750	1017·6	0	24	—	—	0·3	—	—	—	As he did not live to complete the 24 hours, these quantities relate to the urine passed in 18 hours only—the last 18 hours of life. It was loaded with pale lithates.

April 10. For the last month, and especially for the last week, his appetite has been failing and his thirst diminishing in the same proportion. He now eats very little and drinks no more than other people. He had become much weaker, and for the last week has been confined to bed. The bowels are somewhat confined, not having acted for two days. The tongue is moist, and for the first time since the beginning of his illness is coated with a white fur.

The left leg is much swollen with soft œdema which pits deeply and easily.

The veins of the calf are conspicuous, but there is no tenderness in the position of the femoral vein or elsewhere. He was short of breath, respiration 31, pulse 124. He was propped in a half-sitting posture, not being able to lie flat by reason of the cough. The expectoration was copious and almost entirely purulent.

Gurgling sound and amphoric breathing were heard in the right apex, over which percussion elicited a semi-tympanitic tone. This was particularly marked over a space about 2 inches in diameter below the clavicle. Smaller bubbling sounds were heard all over both lungs before and behind. The signs were held to indicate small excavations scattered through both lungs with a considerable vomica at the right apex.

On the morning of the 11th he quietly sank.

Post-mortem Examination.

Over the left hemisphere the frontal bone was tightly adherent to the membranes beneath. On its inner table near the coronal suture appeared a somewhat irregular patch of new bone, about the size of a fourpenny piece, upon and around which the dura mater was firmly attached. The corresponding outer surface of the skull was natural. If, as seemed probable, the change had resulted from a blow, the outer part of the bone had received less permanent injury than the inner—a not unprecedented occurrence.

The arachnoid beneath this spot was adherent to the dura mater, and over more than the anterior half of the brain. This membrane was opaque and dense as if from ancient inflammatory change.

The pia mater was natural in tint, but the superficial cerebral veins were loaded, the vessels in the substance of the brain dis-

tended and conspicuous, and the puncta numerous. The brain was generally watery, and there was a little clear fluid in the ventricles.

Outside the dura mater of the cord was a quantity of gelatinous œdema.

The cord itself—unlike the brain which to naked-eye examination would have passed for natural—presented obvious signs of disease. The central canal was much enlarged and the commissure irregular and changed in texture.

Portions of the brain and cord remitted to chromic acid for minute examination were overtaken by misfortune, and the purpose never accomplished. The foundation of the pathological edifice is therefore wanting.

The lungs were thickly besprinkled with cheesy tubercle-like masses which varied in size from the merest specks up to concretions as large as a walnut. There were also many vomicæ scattered through both, most numerously in their upper lobes. The cavities were largest in the lower part of the upper lobe of the right lung, where two, either of which would have held a large walnut, were in absolute contact with the pulmonary pleura, thus explaining the hyperresonance detected during life.

The liver was increased in size, weighing 68 ounces. It was dense, firm, and of a deep red colour. The kidneys were also enlarged, weighing together 16 ounces; they were generally of a red tint, the cortices being streaked with the yellow lines of tubal distention. One of the cones contained a small collection of thickened pus surrounded by fibroid thickening, but not by vascular injection; it was an ancient abscess such as might have come from pyæmia. A layer of pus, as extensive as a shilling but much thinner, probably from the bursting of a superficial abscess, lay between the kidney and the capsule.

Comments.

In this instance, as so often happens in early life, the disease assumed a severity which left no room for hope that the fatal termination could be long retarded by any means at our command. The loss of sugar on his admission exceeded two pounds daily. The prospects of the patient were further darkened by frequent want of gluten bread, the supply of which was interrupted by the siege of Paris.

The large amount of sugar offered a favourable opportunity for noting the effects of several drugs upon its excretion, and the results, though often negative, are not without interest.

Weekly notes of sugar, urea, phosphoric acid, body-weight, and temperature registered the fluctuations of the disease under varied treatment, and the decline of the patient in spite of all.

Belladonna to the amount of 6 grains of the extract daily left the secretion of sugar precisely as it found it and did not modify the disease in any other particular.

Under arsenic the aspect and strength of the patient improved, though the sugar did not lessen.

The addition of opium was followed, as it usually is, by a diminution of this product.

The further addition of perchloride of iron, suggested by the occurrence of œdema, was immediately followed by the subsidence of the dropsical effusion; and it may be observed that in other cases, as in this, diabetic œdema has been found to be strikingly controlled by iron.

Under the influence of arsenic, together with opium and iron, and such restriction of diet as circumstances allowed, the sugar diminished from 608 grammes to 240; the urea from 85 grammes to 43. The maintenance of the reduction after the substitution of arsenic by strychnia shows that it was not caused by that mineral. It was due probably to the combined effect of diet and opium.

Lactic acid was resorted to with a disbelief in its utility, which was not removed by the observation of any benefit sequent upon it.

The gradual diminution and final absence of sugar was in striking contrast to its former superabundance. Latterly the most delicate testing failed to reveal a trace either in the urine or the expectoration. In such circumstances the sugar ceases from the urine not because it is diverted into another channel, or wholly in consequence of a diminished supply of the necessary material from failure of appetite—for urea is still passed, the elements of which could scarcely be introduced without those of sugar—but probably because the approach of death lessens the impressibility of the nervous system so that it ceases to respond to the irritation which is at the root of the disease.

CASE 2.

Diabetes in advanced life. Benefit from restriction of diet, especially exclusion of milk. Improvement under strychnia. Experimental treatment with lime,

phosphoric acid, belladonna, and iodide of potassium. Effect of vegetable diet on excretion of urea. Gradual blindness, operation for cataract, subsequent gradual sinking. Post-mortem appearances. Characteristic state of brain and cord, liver and lungs, with a peculiar partial dilatation of the hepatic capillaries.

Thomas Kirby, aged 71, well known for many years as the driver of an omnibus on the Hammersmith Road, was admitted under my care at St. George's on December 16, 1871.

His illness dated from the preceding April, when, after a severe attack of pain which shot along the course of the ureter and extended more or less generally over the loins and abdomen, his urine suddenly increased in quantity, insomuch that he had to pass it every quarter of an hour, and became light in colour.

The diuresis was accompanied with much prostration; and the urine was examined and found to be saccharine.

No hereditary tendency to the disease could be traced, nor did its cause appear to be mental, traumatic, or otherwise distinguishable. Except several attacks of rheumatic fever his previous health had been good.

December 16.—On admission his chief complaints were of thirst, dryness of the mouth and of a sweet taste of which he was often conscious. The breath had strongly the characteristic etherial odour of diabetes. He felt weak but could walk about, and his aspect—that of a rather florid old man whose hair, formerly light, was now white with age—was not inconsistent with health. He weighed 8 st. $1\frac{3}{4}$ lbs., his customary weight before his illness having been 10 st. 3 lbs. In the 24 hours ending December 18, he passed 156 grammes of sugar; 35 of urea.

December 18.—His diet was now gradually restricted, bread being first diminished and afterwards withdrawn, gluten bread being substituted. He had also 6 ounces of meat, two eggs, greens, of beef-tea and milk two pints each, and two ounces of gin. Liquor Strychniæ was given every six hours in doses gradually increased from four minims to twelve. This system was continued until February 20. At first he experienced marked improvement, the urine diminished, so that on many days it only measured half what it did on admission, and the sp. gr. fell. But after the first month the improvement ceased and the urine latterly became as copious and as heavy as ever. He had on the

whole lost weight, weighing on February 20th 7 st. 13 lbs., and had become more thin and wrinkled.

February 20.—He complained much of his mouth, which was dry and clammy. The gums were vascular and sore; the teeth loose; the tongue deeply furrowed, dry, and often brown in the centre. The appetite remained excessive. The bowels were usually confined, so that calomel, colocynth pill, and senna draught were occasionally needed. He complained frequently of giddiness; and his memory, possibly from his age, was failing.

I have not reproduced in tedious chronicle the daily variations of the urine. It may be enough to state that from admission until February 20, the quantity ranged from 165 ounces to 80 ounces; the specific gravity from 1,029 to 1,024. In the 24 hours ending February 20 he passed 237 grammes of sugar; 63 of urea. His weight varied from 8 st. 1½ lbs. to 7 st. 10½ lbs.

From February 21 to March 6, the diet remaining practically the same, he was treated with lime in the form of Liquor Calcis Saccharatus, of which a drachm, and afterwards a drachm and a half, were given every 4 hours. Under this he gained 1½ lbs. in weight, but gave no other evidence of improvement. The quantity and specific gravity of the urine remained about the same, and the amount of sugar showed no marked diminution. The only pointed result of this treatment was, as will be seen on reference to the quantitative table, the increased elimination of lime by the kidneys.

From February 21 to March 6, his weight varied from 8 st. ½ lb. to 7 st. 13 lbs. The urine in quantity from 170 oz. to 115 oz.; in sp. gr. from 1,030 to 1,026. He passed in the 24 hours ending March 6, 216 grammes of sugar; 59 of urea.

March 6.—The lime was now exchanged for phosphoric acid, of which to introduce the more, it was given both uncombined and in a neutral salt; a drachm of dilute phosphoric acid and a scruple of phosphate of ammonia every 4 hours.

The only change noted under this treatment was a slight increase in the quantity of urine, which now attained its maximum.

From March 6 to March 30, his weight ranged from 8 st. 1½ lb. to 7 st. 12½ lb.; the quantity of urine from 190 ounces to 120 ounces; the specific gravity from 1,028 to 1,024.

March 30.—Strychnia was now substituted for the phosphate of ammonia and gradually increased.

April 7.—Under the phosphoric acid and strychnia he failed

in health, probably from some cause unconnected with the medicine, which, at other times, suited him. The bowels were sluggish, the appetite absent; he was very low-spirited, complaining that his mouth tasted sweet, and his whole body was parched.

From March 30 to April 10, the urine ranged in quantity from 195 to 110 ounces, and in sp. gr. from 1,028 to 1,025. He weighed 8 st. 1 lb.

April 10.—Without change in the medicine, save augmentation of the strychnia, the milk was withdrawn from the diet and an additional pint of beef-tea substituted. He at once began to amend. He resumed his appetite and equanimity and attained a condition of health of which he had had no experience since the beginning of the disease. He was desirous and, as he thought, able, to resume work, and insisted on leaving the hospital with that view.

From April 10 to June 5, on which day he left, his weight ranged from 8 st. 6 lbs. to 8 st. 3½ lbs.; the daily quantity of urine varied from 120 ounces to 55 ounces, and the specific gravity from 1,025 to 1,019. The sugar in the 24 hrs. ending June 5 amounted to 114 grammes, all symptoms, urinary and constitutional, concurring to indicate improvement.

Out of the hospital he lived not insufficiently but without restriction, and within a month he returned complaining of thirst, weakness, and most of his former troubles. Under strict diet as before, milk being excluded, and with increasing strychnia, he had in the course of a week recovered his comfort though not his weight. This was now 7 st. 9½ lbs. From July 12 to 20 the urine varied in quantity from 110 ounces to 80 ounces; in specific gravity from 1,029 to 1,024.

July 20.—Now again venturing experimentally, I replaced the strychnia by belladonna, cautiously giving the extract in doses which mounted from a third of a grain to five grains three times a day. This was continued with no noticeable effect until on August 12, after taking 15 grains a day for six days, he complained of giddiness which made him walk somewhat unsteadily, but ceased when he lay down. There was also a slight injection of the skin like a faint scarlatinal eruption; this was general but especially well marked about the abdomen. These were the only definite effects of the belladonna. The temperature was not increased (98·4). The pupils were not enlarged.

The throat was not dry, though he complained of the mouth as 'sticky.' The tongue was clean and moist; the appetite and bowels unaffected; the pulse somewhat bounding, as before in rate (80).

The daily measurement of urine under the belladonna varied from 110 to 75 ounces; the specific gravity from 1,027 to 1,021.

August 14.—The strychnia was resumed on August 14 and continued until September 16, by which date he was taking 40 minims a day of the liquor. On the discontinuance of the belladonna he lost his giddiness, and under the strychnia quickly resumed his former condition of quiescence and comfort.

From August 14 to September 16, the urine ranged in quantity from 100 to 45 ounces; in sp. gr. from 1,033 to 1,026. His weight varied from 7 st. 12¼ lbs. to 7 st. 12½ lbs.

In the 24 hours ending September 17 he passed 116 grammes of sugar, almost the same as when last estimated three months before. The urea amounted to 52 grammes.

September 17.—With this standard I determined to try iodide of potassium, moved thereto by the good sometimes wrought in chronic diseases of the nervous centres by this salt either alone or with strychnia. Ten grains were ordered every six hours, to which, as the medicine caused some looseness of the bowels, ten drops of laudanum were shortly added.

October 23.—This was continued until October 23, by which date the sugar had fallen to 61 grammes; the urea to 34. Under the iodide his weight had ranged from 7 st. 10½ lbs. to 7 st. 8½ lbs., the lowest weight being at the conclusion of the course. The urine from 90 to 30 ounces; of from 1,031 to 1,025 in specific gravity. The only observable difference in his state of health was, save the slight loss of weight, that the bowels were freely open instead of being as formerly constipated. The diminution of sugar and urea was striking. It remained to determine how far it was due to the iodide and how far to the small quantity of laudanum associated with it—a question which other cases may answer.

October 24.—Augmented strychnia now replaced the mixture in question; and, to cut short a part of the case marked by monotonous good health, he continued under its influence, either alone or with phosphoric acid, until the following April. He now looked better in every respect than formerly. He weighed 8 st., a gain of 5½ lbs. since October. He had a florid healthy com-

plexion, and no longer complained that his mouth was parched or sweet. The tongue was moist, the bowels acted daily and naturally. He no longer suffered from thirst; drinking generally a little water in the night but none in the day as had been his wont. He lengthened his walks abroad, and in his own phrase 'did not feel as if he had anything the matter.' As the single drawback, he said that his eyes were failing, but nothing amiss could be seen, and there was as yet no evidence of other than senile change.

For some time past his gums had been shrinking, and the teeth becoming denuded and loose. He had recently lost several and was now nearly toothless.

His own sense of health, with the general impression produced by his fresh colour and active habits, made it impracticable to retain him longer in the hospital, and he was accordingly dismissed in April 1873. The more natural state of the urine may be sufficiently gathered from the fact that during the last two months of his treatment the quantity varied from 60 to 25 ounces; the specific gravity from 1,024 to 1,018; all concurring to display the disorder in a state of less activity than in any previous epoch.

July 14, 1873.—In the following July he reappeared and was taken into the hospital for the third and last time. His chief complaint now was of increasing loss of sight due to double cataract which had become apparent since he was last a patient. The thirst and diuresis had to some extent returned, but subsided under diet and strychnia.

September 1873.—He was now subjected to an experiment, harmless in its brevity, partly in view to which he had been readmitted.

All medicine being withdrawn, his habitual highly nitrogenous diet was substituted for three days by one chiefly amylaceous and saccharine. That the excretion of sugar would be thereby greatly increased was foretold by common experience; but I was desirous to examine the influence upon the urea of a diet supplying a minimum of its nitrogenous staple.

His habitual diet consisted of 8 ounces of meat, 4 eggs, 2 pints of beef-tea, greens, gluten bread, and gluten flour to mix with his beef-tea. The diet interposed for three days consisted of common bread, arrowroot, sago, tapioca, potatoes, 2 ounces of sugar and 3 pints of milk; being, with the exception of the milk, entirely of vegetable origin.

The results are stated in detail below. In brief they amounted to a great increase of urinary sugar and water, while the urea, notwithstanding the diminished supply of its distinguishing element, was discharged for the three days with scarcely any abatement. On the third day it was slightly lessened, and had the experiment been lengthened, which consideration for the patient forbade, it would probably have undergone a more marked diminution.

September 17.—The cataract, which of late had increased in both eyes so as to render him so nearly blind that he could not walk about without being led, limited his exercise, depressed his spirits, and seemed so seriously to threaten his general health by the deprivation of air and exercise which it involved, that I yielded, perhaps unwisely, to his own earnest wish for surgical relief. Mr. Brudenell Carter removed the lens from the left eye with admirable success as far as the immediate surgical results were concerned. The wound healed rapidly and perfectly without any local change that could have been wished otherwise, but his depression increased after the operation while he lay in bed with eyes bandaged, and was not materially lessened by the admission of light and considerable restoration of vision. He complained of weakness and loss of appetite, but of no more definite pain or discomfort. Tonics and stimulants produced no response; and though he was tempted with an unlimited variety of food, he found no return of appetite. He quietly sank and died without previous unconsciousness on October 6, at the age of 73.

Urinary Constituents passed in 24 Hours.

Date	Quantity	Specific Gravity	Sugar	Urea	Proportion of total Urea to Sugar 1 to —	Proportion of excess of Urea to Sugar allowing 3 grammes to a stone 1 to —	Albumen	PO_5	CaO	(2MgO)'
			No Treatment or Restriction.							
	C.C.		grms.	grms.	grms.	grms.		grms.	grms.	grms.
1871. Dec. 18	2970	1028·5	156	35	4·4	14·1	0	2·2	·117	—
			Diabetic Diet and Strychnia.							
1872. Feb. 20	5110	1025·7	237	63	3·7	6·0	trace	2·5	·370	·118
			Diabetic Diet and Lime.							
Mar. 6	4540	1025·6	216	59	3·6	6·1	—	—	·755	·106

Date	Quantity	Specific Gravity	Sugar	Urea	Proportion of total Urea to Sugar 1 to —	Proportion of excess of Urea to Sugar allowing 3 grammes to a stone 1 to —	Albumen	PO_5	CaO	$(2MgO)$[1]
Diabetic Diet and Phosphoric Acid and Strychnia.										
	C.C		grms.	grms.	grms.	grms		grms.	grms.	grms.
1872. June 5	3410	1023·1	114	—	—	—	—	—	—	—
Left Hospital.										
Diabetic Diet.										
1872. Sept. 17	3260	1023·1	116	52	2·2	4·1	—	—	—	—
Diabetic Diet. Iodide of Potassium.										
1872. Oct. 23	2270	1019·5	61	34	1·8	6·1	—	1·58	·526	·096
Left Hospital.										
Animal (Diabetic) Diet.										
1873. Aug. 27	3950	1022	188	51	3·2	6·1	—	—	—	—
28	3800	1022	180	79			—	—	—	—
29	4640	1028	256	83			—	—	—	—
30	4710	1021	235	56			—	—	—	—
31	4070	1022	193	48			—	—	—	—
Average of preceding 5 days	—	—	210	65	3·2	6·1	—	—	—	—
Vegetable Diet.										
1873. Sept. 1	5570	1020	293	50	6·4	14·0	—	—	—	—
2	6360	1008	244	44			—	—	—	—
3	5670	1025	315	39			—	—	—	—
Average of preceding 3 days	—	—	284	44	6·4	14·0	—	—	—	—
Animal (Diabetic) Diet.										
1873. Sept. 4	4800	1020	240	43	4·3	9·6	—	—	—	—
5	3720	1020	177	44			—	—	—	—
6	4390	1020	209	48			—	—	—	—
7	3600	1020	144	40			—	—	—	—
Average of preceding 4 days	—	—	192	44	4·3	9·6	—	—	—	—
Not strictly Dieted. Approach of Death.										
1873. Oct 5	1120	1025	43	—	—	—	trace	·33	·397	·112

[1] The lime and magnesia were in all cases estimated by precipitation from the ash which was found to give better results than the fresh urine.

The sugar, urea, and phosphoric acid were estimated volumetrically.

Post-mortem Examination.

Brain.—The dura mater was adherent to the convolutions for a small space at the summit of each hemisphere; the arachnoid was mottled with opacity; the pia mater generally injected.

The substance was firm throughout, the increase of consistence being especially evident in the tenacity of the septum lucidum and neighbouring parts. The ventricles were natural; they together contained about a drachm of fluid.

Many parts of the white matter were conspicuously cribriform, displaying groups of dark spots or pores which ranged up to about the size of mustard seeds; some were empty, others had in their centre what looked like a fine bristle and was obviously an altered blood vessel. Many districts were entirely devoid of these pores; in others they were closely set, scores lying within the space of a square inch. They were especially numerous between the floor of the lateral ventricles and the base of the brain, including the corpora striata and the white matter of the inferior convolutions. The microscope showed these excavations to be similar to those described in every preceding case. As in the case of Stewart (Plate II.), they were most marked in the white matter of the convolutions. The cavities were rugged tunnels, in which lay disproportionately minute vessels, nervous débris, and crystals of hæmatine. Speaking anatomically, these were partial and irregular enlargements of the perivascular canals. At one spot where no cavity existed considerable masses of hæmatine were imbedded in the brain substance outside a small vessel. They probably had resulted from hæmorrhage thence not sufficiently abundant to cause destruction of tissue. This observation is of interest as according with evidences in a more recent stage of the hæmorrhagic origin of the excavations. (See fig. 4, page 35.)

The cord presented no unnatural appearances to the naked eye excepting injection of the superficial vessels. The microscope, however, showed changes of the same kind, and fully as extensive, as in any previous case. The vessels in the anterior fissure, along its whole length, were irregularly swollen; the fissure itself was eroded sometimes to the severance of the white commissure at its base; the erosions followed the vessels through the commissure to the production of large holes at each extremity; and in many instances the excavations were packed with blood and

débris, nervous and vascular, while in others they were empty. In a few places the anterior horns were penetrated by vessels exaggerated similarly to those described.

The liver weighed 52 ounces. It was generally deeper in colour and redder than natural with a large mottling of a yellowish tint. The texture was firm, elastic, and more than naturally uniform from indistinctness of the acini. The organ generally was loaded with blood, and the appearance much like that produced by the venous congestion of cardiac disease. The bile was dark green.

The microscope showed distention and partial thrombosis of the portal venous system. Blood had solidified in many of the portal and accompanying arterial branches; in some instances from the changes which the clot had undergone it had clearly been deposited some time before death. Some of the obstructed portal canals were one eighth of an inch in diameter, others more minute.

The condition of the portal system was almost exactly that represented in woodcut 13 (page 49), which was taken from the liver of another person who died of the same disease. The system of venous exit displayed abnormities of a more exceptional character, a similar coagulation apparently causing, in certain parts of the organ, striking and to me novel appearances. These consisted of patches of a remarkable spongy transformation, which proved to be due to an extravagant dilatation of the capillaries belonging to the hepatic vein. Their cavities were swollen to the compression and atrophy of the intervening glandular structure; no more remaining of the hepatic epithelium than sufficed to form the threads of the open network of which the enlarged capillaries constituted the interspaces.

Further particulars of this remarkable change, illustrated by some drawings, are given in the general sketch of the pathology of diabetes (page 50).

The apex of the right lung was in a state of peculiar solidification; a grey mottling exuding pus on pressure, apparently chronic grey hepatisation, lying in patches separated by œdematous tissue. A few small cavities were found in the hepatised patches. Under the microscope the air-cells in the affected part were filled with a corpuscular pneumonic product such as is represented in woodcut 17, page 55.

In the neighbourhood of the cells thus affected was much

fibroid thickening, especially under the pleura. This was much dotted with pigment.

The kidneys were of unequal size. The right weighed 3 ounces; it was greatly contracted, cysted, and granular; the left weighed 7 ounces; it was nearly smooth, with a thickened and somewhat yellow cortex in which were a few cysts.

The heart weighed 11 ounces, the mitral valve was slightly thickened, the aorta was dilated but nearly natural.

REMARKS.

The benefit here received from a diet rigidly exclusive of starch and sugar was as usual great. The loss of the milk which up to a certain point formed part of the fare was an enduring gain. The sugar with which whey abounds renders this portion of milk at least especially undesirable in diabetes. As to medicine, the whole course of the case gave evidence of the value of strychnia. Under somewhat less than half a grain a day, cautiously reached and long continued, the general health was maintained and the excretion of sugar slowly lessened.

Holding to the diet without variation, I ventured upon several therapeutical experiments, substituting the strychnia for a time by other drugs, taking care not to push them to injurious lengths. I thus tested the action of lime, phosphoric acid, belladonna, and iodide of potassium. The iodide alone seemed to touch the sugar, I will not say to do good, its administration guarded with a small quantity of laudanum being attended with a marked diminution of this constituent of the urine. The opium, however, complicated the experiment; and even at best the patient, after its discontinuance and the resumption of the strychnia, attained a better condition than he had reached under the iodide.

His death, after a trifling and apparently successful operation, is an instance of the feeble grasp of life which a diabetic patient has.

The post-mortem appearances as far as regarded the nervous centres, the liver, and the lung were such as are constantly met with in diabetes; with the exception, however, of the extraordinary capillary dilatations in the liver, of which my experience has given no other instance.

The condition of the kidneys was probably antecedent to, and quite unconnected with, the disease of which he died.

CASE 3.

Severe diabetes from mental shock. Effects of cannabis indica, sugar, and starch. Extraordinary excretion of lime in the urine. Post-mortem display of extensive and characteristic cerebral lesions.

Ann Mackay, a freckled sandy-haired woman with rather a worn look, came to St. George's Hospital on April 22, 1871, suffering, as she had been told, from debility. Her aspect was suggestive of diabetes, and a few questions which promptly elicited parching thirst, rapid wasting, and excess of urine, removed all doubt from the nature of her disorder.

She was 35 years of age, the mother of 10 children, by profession an ironer.

Her health had always been good until a certain day in the preceding August, on which she was suddenly made aware that one of her children had fallen out of a third-floor window and been taken up for dead from the pavement below.

The child survived ; but the fall was fatal to the mother.

From this hour her health was destroyed. For three weeks she could, as she expressed it, neither eat nor sleep. Within two months of the accident she found she was getting thin and was passing a large quantity of water, a drop of which if it fell on her dress 'stiffened like so much sugar.' At the same time she had 'a feverishness' chiefly manifested by a raging thirst unquenched by quarts of water, while the mouth and throat became dry and the tongue cracked. She did not lose her appetite nor was it notably increased.

For the last six weeks before her admission menstruation had been excessive.

April 22, 1871.—When admitted her features were sharpened, but the face was not unnatural in expression. The skin was dry and powdery ; the tongue moist, red, smooth and free from coating. The bowels were confined. The pulse was 124. She had no cough. Her weight was 7 st. 4 lbs. 2 oz. It was ascertained that twelve months previously she had weighed 10 st. 11 lbs. ; having lost $3\frac{1}{2}$ st. apparently within 8 months, certainly within a year.

April 28.—She was placed upon a partially restricted diet, from which sugar, beer, and potatoes were excluded, comprising

2 chops, 3 eggs, a pint of beef-tea, greens, one loaf of common hospital bread, and a quarter of a pint of milk with tea. This on May 7 was modified by the substitution of gluten bread for the hospital loaf, and the diet thus modified was continued to the end with certain temporary additions which will be specified.

As medicine, cannabis indica was put to the trial, the extract being given every 6 hours, in doses which were gradually increased from a quarter of a grain to 5 grains, from the time of her admission until June 2.

While under the cannabis indica, arrowroot and sugar were introduced, each for a few days, with results which will appear in the following columns.

Cannabis Indica and partially restricted Diet (Meat, Eggs, Greens, Beef-tea, Common Bread, and ¼ pint Milk).

	Treatment	Quantity of Urine	Specific Gravity	Sugar	Urea	Phosphoric Acid	Lime (CaO)	Magnesia (2MgO)	Body Weight	Temperature	Remarks
		C.C.		grms.	grms.	grms.	grms.	grms.	st. lb. oz.		
April 28	Ext. Cannab. Ind. gr. ½ 6tis horis	5050	1040·3	421	63	4·5	—	—	7 4 2	98·0	—
„ 29	Ext. Cannab. Ind. gr. 1	4600	1041·2	418	55	3·2	—	—	—	100·0	—
„ 30	Ext. Cannab. Ind. gr. 1½	4820	1038·6	371	57	—	—	—	—	—	—
May 1	—	4540	1037·7	324	59	—	—	—	7 2 9	100·3	—
„ 2	Ext. Cannab. Ind. gr. ij	4270	1038·7	316	64	—	—	—	7 2 9	—	—
„ 3	Squire's extract gr. i.	4480	1038·0	344	58	—	—	—	—	—	—
„ 4	—	3840	1038·5	284	61	—	—	—	—	—	—
„ 5	—	3860	1038·7	286	77	—	—	—	—	—	—
„ 6	Squire's extract gr. 1½	4200	1036·6	289	71	—	—	—	—	—	—

Averages of preceding 9 days :—Sugar 339 grammes, urea 62 grammes, proportion of total urea to sugar 1 to 5·4, proportion of excess of urea to sugar 1 to 8·2.

Cannabis Indica and Strict Diabetic Diet (Gluten Bread substituted for Hospital Loaf).

Date	Treatment	Quantity of Urine	Specific Gravity	Sugar	Urea	Phosphoric Acid	Lime (CaO)	Magnesia (2MgO)	Body Weight	Temperature	Remarks
		C.C.		grms.	grms.	grms.	grms	grms.	st. lb. oz.		
May 7	—	4810	1038·5	331	62	—	—	—	7 7 0	—	—
,, 8	Squire's extract gr. ij.	3420	1035·7	190	71	—	—	—	—	—	The general symptoms unchanged. None attributed to Cannab. Ind. except slight morning headache. Slept better than at home, and dreamed more. Less thirsty, mouth less dry.
,, 9	—	3450	1036·9	215	65	—	—	—	7 4 0	—	—
,, 10	—	3340	1037·6	202	76	—	—	—	—	—	—
,, 11	—	3510	1037·4	195	77	—	—	—	—	—	—
,, 12	—	3390	1035·2	182	74	—	—	—	—	—	—
,, 13	Ext. Cannabis Ind. gr. ij ½	3530	1036·5	207	81	—	—	—	—	—	—
,, 14	—	3810	1031·6	195	80	—	—	—	—	—	—

Averages of preceding 7 days (May 7 excluded, as on that day change of diet was only partial):—Sugar 198 grammes, urea 74, proportion of total urea to sugar 1 to 2·6—of excess of urea to sugar 1 to 3·7.

As before, with addition of Four Ounces of Loaf Sugar Daily.

Date	Treatment	Quantity of Urine	Specific Gravity	Sugar	Urea	Phosphoric Acid	Lime (CaO)	Magnesia (2MgO)	Body Weight	Temperature	Remarks
		C. C.		grms.	grs.	grms.	grms.	grms.	st. lb. oz.		
May 15	—	4120	1033·9	235	86	—	—	—	7 8 8	—	—
" 16	Ext. Cannab. Ind. gr. iij.	4820	1036·9	344	81	—	—	—	—	—	—
" 17	—	3740	1037·0	241	71	—	—	—	—	A.M. 99·4 P.M. 99·2	—
" 18	—	4680	1035·9	283	88	—	—	—	—	—	—
" 19	Ext. Cannab. Ind. gr. iv.	5000	1034·6	294	100	—	—	—	—	—	—
" 20	Ol. Ric. ℥ss. p. r. n.	4800	1036·7	309	91	—	—	—	—	—	—
" 21	—	5340	1036·8	428	96	—	—	—	—	—	General symptoms unchanged.
" 22	—	5460	1035·8	341	98	—	—	—	7 7 4	—	—

Averages of preceding 7 days (May 15 excluded, as day of change):—Sugar 308 grammes, urea 89 grammes, proportion of total urea to sugar 1 to 3·4—of excess of urea to sugar 1 to 4·5.

Four Ounces of Arrowroot daily instead of Sugar.

Date	Treatment	Quantity of Urine	Specific Gravity	Sugar	Urea	Phosphoric Acid	Lime (CaO)	Magnesia (2MgO)	Body Weight	Temperature	Remarks
		C.C.		grms.	grs.	grms.	grms.	grms.	st. lb. oz.		
May 23	Ext. Cannabis Ind. gr. v.	6000	1035·0	375	102	—	—	—	—	A.M. 99·2 P.M. 99·0	—
„ 24	Ext. Cannab. Ind. Squire's) in form of tincture, gr. v. 6tis horis	4450	1036·7	278	80	—	—	—	—	—	Weather very hot, much sweating.
„ 25	Haust. Sennæ, p. r. n.	5160	1037·3	322	103	—	—	—	—	—	Sleeps much—woke for food and medicine. No headache. Mind quite clear. No tremor or especially nervous symptom beyond drowsiness. Tired, weak feeling especially in legs. Tongue natural; pulse 88. While under arrowroot has complained much of thirst.
„ 26	—	4900	1037·0	316	88	—	—	—	—	—	—
„ 27	—	4740	1037·7	316	94	—	—	—	—	—	—

Averages of preceding 5 days:—sugar 321 grammes, urea 93 grammes, proportion of total urea to sugar 1 to 3·4, proportion of excess of urea to sugar 1 to 4·4.

Recommenced Four Ounces of Sugar daily instead of Arrowroot.

Date	Treatment	Quantity of Urine	Specific Gravity	Sugar	Urea	Phosphoric Acid	Lime (CaO)	Magnesia (2MgO)	Body Weight	Temperature	Remarks
May 30	—	5600	1036·9	386	89	—	Average of 2 days 2·76	—	7 8 9	A.M. 99·4 P.M. 99·4	—
„ 31	—	4950	1036·1	330	84	—		—	—	—	—

Averages of preceding 2 days:—Sugar 358 grammes, urea 86 grammes, proportion of total urea to sugar 1 to 4·1, proportion of excess of urea to sugar 1 to 5·5.

Strict Diabetic Diet as before Sugar and Arrowroot Experiments.

Date	Treatment	Quantity of Urine	Specific Gravity	Sugar	Urea	Phosphoric Acid	Lime (CaO)	Magnesia (2MgO)	Body Weight	Temperature	Remarks
		C.C.		grms.	grs.	grms.	grms.	grms.	st. lb. oz.		
June 1		5300	1036·9	359	—	—	—	—	—	—	—
„ 2	Cannab. Ind. discontinued, replaced by strychnia, which was continued to the end	4800	1037·3	320	81	4·8	—	—	—	—	Much as at last note.
„ 3	—	3960	1038·7	264	71	—	—	—	—	—	Trace of albumen. Sleeps rather heavily. Appetite not so good. Palpitation and pain in side. Tongue clean but feels sore. Skin cool, pulse 108.
„ 4	—	4160	1032·9	198	—	—	3·19	—	—	—	—
„ 5	—	4980	1033·1	212	104	—	[1]3·38	[1]·52	7 5 4	—	—
„ 6	—	4140	1031·3	197	76	—	—	—	—	A.M. 94·4 P.M. 95·0	—
	—	4750	1031·9	206	90	2·8	—	—	—	—	Less sleepy. Feels better under Strychnia than under Can. Ind.
„ 8	—	4630	1033·2	243	83	—	—	—	—	—	Albumen slightly increased, not enough to give flakes or separable deposit.
„ 9	—	4250	1031·3	184	89	—	—	—	—	—	—
„ 10	—	4550	1028·4	185	79	1·3	—	—	—	—	—

Averages of preceding 10 days:—Sugar 236 grammes, urea 84 grammes, proportion of total urea to sugar 1 to 2·8—excess of urea to sugar 1 to 3·7.

[1] Lime and magnesia here estimated from ash. In other estimations precipitated directly from the urine.

Averages of Sugar and Urea passed in Twenty-four Hours under various Diets.

Diet	Sugar	Urea	Total Urea to Sugar as 1 to —	Excess of Urea to Sugar allowing 3 grammes to a stone as 1 to —
Partially restricted . .	339	62	5·4	8·2
Strict diabetic . . .	198	74	2·6	3·7
Diabetic + loaf sugar . .	308	89	3·4	4·5
,, ,, arrowroot . .	321	93	3·4	4·4
,, ,, loaf sugar .	358	86	4·1	5·5
Strict diabetic . . .	236	84	2·8	3·7

On the night of June 10, the patient was attacked with vomiting, but nevertheless went out walking on the following day according to her custom. She returned complaining much of discomfort in the bowels; and it was ascertained, what the patient had previously withheld, that there had been no evacuation for nine days. Under a powder containing three grains of calomel and an enema the bowels acted, but the vomiting, though not severe or frequent, continued in spite of effervescing saline draughts, and the patient assumed a worn look, her eyes sank, and she went to bed on the 12th saying she felt very tired and looking weary and worn out. From this time she gradually sank, and quietly expired, without pain or loss of consciousness, on the morning of the 13th.

Post-mortem Examination.

The friends of the patient raised objections to a post-mortem examination; permission to open the head was obtained under promise of not going further.

The meninges and the brain generally were much congested, but beyond increased vascularity no changes were detected with the naked eye.

It is not necessary to describe the microscopic appearances of the brain in general detail; changes similar to those noted in the other cases were widely scattered. At the base the morbid appearances were especially marked, and furnished the subjects of the woodcuts numbered 8, 9 and 10 on pages 39 and 40. Large holes like those of Gruyiere cheese were seen in the corpora striata and optic thalami, more particularly near the edges of the optic tract. These were striking objects to the naked eye; many were as large as peas, and in their number and approxima-

tion involved a considerable destruction of tissue. In one of the cuts referred to the actual size of the excavations is shown. Some were empty, others contained entangled arteries, others a peculiar elastic translucent substance, delicately fibro-nucleated. The illustrations at pages 39 and 40 may make further description unnecessary. The entangled blood vessels which some of the cavities contained were wrapped in an irregular web of connective tissue which was thickly besprinkled with shining crystals of hæmatine. In some were large degenerate nerve cells, which retained their outline though separated from their connections. The gelatinous material which filled some of the hollows was delicately striated, as if derived from white nervous tissue, and still contained many minute blood vessels. It was compressible, yielding before the edge of the razor, so that it needed some care to include it in the sections. In appearance it was abruptly separated from the natural brain tissue, which formed the edges of the cavity; in structure it was continuous with it. I have found the same gelatinous material in other diabetic brains, particularly after the more rapid forms of the disease. It is probably the result of a circumscribed transformation of the white matter. (See lithograph referring to case of Salisbury, plate I.)

Commentary.—In this case the mental origin of the disease was sufficiently definite. The disorder was unusually severe, and the pathological lesions as discovered after death were correspondingly distinct and extensive.

The toleration of cannabis indica was remarkable, the patient taking for a long time 20 grains a day of the best obtainable extract. Under its influence it is to be observed that the temperature never went below 99·0 ranging exceptionally high for severe uncomplicated diabetes. On the discontinuance of the drug the temperature fell 5 degrees.

This remarkable variation cannot however be attributed to the medicine, since I have given more than twice the quantity without any alteration whatever in the thermometric range. Other than thermometric the only results traced to this potent remedy were drowsiness and some flushing of the face. Like all drugs, with the exception of opium and its derivatives, and iodide of potassium, cannabis indica appeared to exert no action upon the secretion of sugar.

With regard to the intrusion into the diet of sugar and arrowroot, the correspondingly increased exit of sugar probably always

present in such circumstances was instructively shown by the analyses. The urea at the same time was somewhat increased; not that we can suppose an increased formation of this nitrogenous substance to be determined by the hydrocarbons in question, but probably because it was more freely removed by the diuresis which they occasioned. A temporary increase of urea may thus ensue in connection with an increase of saccharine diuresis even though the nitrogenous elements of food may be withdrawn to be replaced by sugar and starch. This is exemplified in the cases of Kirby and Howel (pages 163 and 178).

The point in this case however, which chiefly entitles it to separate record is the unexampled discharge of lime with the urine.

In observations made on various persons and disorders rather by chance than design, I found an excessive escape of this earth by the urine associated with nervousness, mental agitation, and other disturbances which I could not characterise more definitely than as nervous irritation or excitement. Whether or not such terms are justly descriptive, I could not doubt that the quantity of lime in the urine was directly swayed by the nervous system. And regarding diabetes as a form of cerebral irritation, I was led to enquire into its influence upon the elimination of this urinary ingredient. I found it to be always exaggerated, though in no other instance so greatly as in this, where it was multiplied at least tenfold.

The solubility of lime in syrup suggested that the earth, simply dissolved out by the diabetic sugar, might find exit as a saccharate, its quantity depending on the quantity of sugar discharged. I found however by comparing various cases that the variations of lime and sugar were independent of each other, and that the loss of lime was due, not to this disorder of the secretion, but probably rather to disease of the brain. In the instance under consideration it will be noted that less lime escaped while the urinary sugar was enhanced by saccharine food than subsequently when it was controlled by diet.

Case 4.

Chronic diabetes. Effects of animal and vegetable diet upon the urine. Experiments with cannabis indica and iodide of potassium.

Joseph Howel, a parish schoolmaster at Cold Norton, the

father of James Howel whose death from diabetes has been already related, began about Michaelmas 1871 to pass water in increased quantity shortly followed by thirst and wasting. In August 1873, then aged 63, he became my patient in St. George's Hospital. His condition, one of not very severe diabetes in a chronic form, presented nothing worthy of especial record. The case has been reported only for the sake of some dietetic and pharmaceutical experiments made in the course of it.

The usual diet of diabetes—meat, beef-tea, eggs, greens, gluten bread and gluten flour—was exchanged for three days for a vegetable one consisting of common bread, potatoes, arrowroot, sago, tapioca, milk, and two ounces of sugar, and the former regimen then restored.

The results as far as the urine is concerned are as follows. It must be stated that the specific gravity was taken with the float, not with the balance; the results, however, may be nearly trusted.

Date	Quantity	Specific Gravity	Urea	Sugar
Animal (Diabetic) Diet.				
	C.C.		grammes	grammes
August 24	2,050	1,021	38·9	76
,, 25	2,390	1,022	43·0	104
,, 26	3,110	1,030	49·7	155
,, 27	2,910	1,028	52·3	162
,, 28	3,100	1,026	55·8	173
,, 29	3,550	1,024	39·0	169
,, 30	2,280	1,029	36·4	134
,, 31	4,450(?)	—	—	—
Averages of preceding 7 days	2,962	1,025	45	139
Vegetable Diet.				
September 1	6,950	1,008	62·5	316
,, 2	7,080	1,015	53·1	332
,, 3	5,900	1,005	41·3	281
Averages of preceding 2 days	6,490	1,010	47	306
Animal Diet.				
September 4	4,420	1,026	46·4	294
,, 5	3,940	1,027	47·2	262
,, 6	4,100	1,027	57·4	273
,, 7	3,650	1,028	44·7	228
Averages of preceding 3 days	3,896	1,027	49	254

Date	Quantity	Specific Gravity	Sugar	Urea
Diabetic Diet unvaried throughout.				
Without Medicine.				
	C.C.		grammes	grammes
November 27 . . .	4,100	1,030	292	—
Iodide of Potassium from November 27 to December 14.				
December 14 . . .	750	1,038	51	—
Without Medicine.				
January 28	3,700	1,029	238	59
Iodide of Potassium from January 28 to March 10.				
March 10	1,820	1,032	110	34·5

The immense increase of sugar and water under the vegetable regimen is consistent with ordinary experience. It is to be noted also that the urea increased in the same circumstances probably in consequence of the enhanced diuresis. These facts are displayed diagrammatically at page 226.

It is worth noting that the exaggeration of glycogenesis produced by the starchy diet had not completely subsided four days after its discontinuance.

He lost weight and strength under vegetable diet, but speedily recovered both. At the same time his legs were observed to be œdematous, which condition gradually subsided, as it usually does, under perchloride of iron.

As supplementary to the preceding estimations, I may state that on September 20, the urine amounting to 6500 C.C., the ash was examined for the earths. The 24 hours' urine gave ·962 of lime; ·243 of magnesia; a considerable excess particularly of lime.

Maintained in good health by means of strychnia and cod-liver oil, these remedies were experimentally withdrawn and cannabis indica substituted in doses gradually increased up to seven grains every four hours. With this quantity he had slight frontal headache and some giddiness equally whether standing or lying. He staggered in walking especially in turning round. The pupils were nearly unaffected but were thought to be a trifle smaller than when the narcotic was commenced. The appetite remained good; the quantity and degree of saccharinity of the urine practically unchanged and until the dose reached 42 grains of the

extract daily the effects of this potent drug were chiefly remarkable by their absence. With iodide of potassium, as in other cases in which I have used it, the effects were sufficiently marked.

On two occasions I gave a course of this salt at the rate of 40 grains a day. The diminution of sugar as seen by the annexed observations (Table) is sufficiently striking, but not more so than the extreme prostration which in each trial followed the remedy. This was such as to be immediately dangerous. Appetite failed simultaneously but apparently not to a sufficient degree to explain either the failure of strength or the diminution of sugar. It is to be observed that the effect of the iodide in controlling the glycosuria is only temporary, it does nothing towards curing the disease.

In July 1874 he left the hospital with incipient cataract in both eyes, but otherwise much as when he entered it.

CHAPTER VIII.

DIABETES INSIPIDUS.

Synonyms. Diabetes insipidus, polyuria, hydruria, urinæ profluxio, and polydipsia are terms which have been applied to a disorder of which the characteristic symptom is an extravagant flow of watery urine, sugar being absent, and dilution its chief peculiarity. Of these denominations the last is inappropriate, forasmuch as the vice of the disease is not in the introduction but the expulsion of water. It is not that the person affected drinks beyond the wants of the system, and discharges the excess by the kidneys; but that he urinates more than is proper to his condition and drinks to supply the loss. And of the names expressive of urinary superflux, perhaps *diabetes insipidus* is the best since it implies alliance or analogy with diabetes mellitus, a suggestion with which our advancing knowledge is accordant.

Physiology.

In brief, our present physiological knowledge as relating to this disorder—somewhat less ample than with diabetes mellitus—amounts to this.

Within the medulla oblongata lie the centres which rule the glandular action, or in other words regulate the calibre of the blood vessels, both of the liver and of the kidney. If irritation be brought to bear upon either of these spots, possibly either by changes in themselves or by irritation directed upon them from without, the subject vessels dilate; when the irritation falls upon the hepatic

centre glycosuria results, when upon the renal hydruria. The nervous route from the medulla to the liver has been accurately mapped; with regard to the kidney there is more doubt.

Influence of medulla.

Bernard, to whom the obligations of physicians are never ending, showed that while puncture of one part of the medulla made the urine saccharine, puncture of another part made it simply superabundant.

When the floor of the fourth ventricle[1] was punctured in the middle line between the origins of the auditory and pneumogastic nerves, the urine became both saccharine and profuse. Pricked a little higher, the urine failed to display sugar but became superabundant and often albuminous. Lower, the secretion became saccharine without increase of its quantity. Hence he inferred that the higher region bore relation to the function of the kidney, the lower to that of the liver, while the intermediate spot told upon both glands, causing the urine from exaggerated renal circulation to increase, and from exaggerated hepatic circulation to acquire sugar.

Other experimenters, among whom Eckhardt must be mentioned, have confirmed the observation that either hydruria or glycosuria may result from punctures of the medulla, though with the belief that the source of each is not to be so strictly limited as Bernard supposed.

Of cerebellum.

The application of chemical irritants to the middle lobe of the cerebellum has been found to cause hydruria, in most instances unaccompanied by the production of sugar, the latter result to be always prevented by section of the nerves of the liver before irritating the nervous centre.[1]

Of nerves.

It has been found further that in the dog, section of the splanchnic nerves causes the urine to become profuse; and that if this nerve be divided only on one side the corresponding kidney is the source of the exaggerated secretion. The secretion is arrested by irritation of the

[1] 'Leçons de Physiologie Expérimentale,' vol. i. p. 339.

peripheral end of the divided nerve. It has been stated by Bernard that irritation of the pneumogastric has a contrary effect to that of the splanchnic, and increases the flow. According to this the splanchnic is the nerve which as touching this gland contracts vessels and lessens secretion; the pneumogastric causing, on the contrary, dilatation and discharge. Thus, for the renal secretion, the splanchnic is the inhibitor, the pneumogastric the excitor; and hyperflux may result either from paralysis of the former, or irritation of the latter.

PATHOLOGY.

That the amount of urine is influenced in the human subject by the nervous system is obvious to the most superficial observation; hysterical urine, abundant pale and watery, much like that of diabetes insipidus except that its characters are more transient, is of old experience. And the urine of nervous agitation, more especially if it be accompanied by sleeplessness, is of the same sort.

Many instances are recorded in which brief or lasting profusion of urine has succeeded upon injuries of the head, or intracranial disease.

Polyuria consequent upon injuries of the head.

As consequent upon injury, M. Fischer[1] has brought together four instances of *simple polyuria*, as he terms it, or of superabundance without saccharinity of urine. In all the symptoms followed immediately upon, and were apparently due to, the hurt.

In one case the injury is described somewhat vaguely, as a blow on the right side of the head from a beam; in each of the others the front of the head was the part struck; in one, a man fell from a height, and received a contused wound over the frontal bone; in another, a fall resulted in a compound fracture of the frontal bone; in the third, the forehead was severely wounded by a kick from a horse. In all the quantities drunk and passed

[1] 'Archives Générales de Médecine,' 1862, vol. ii. p 418.

were very large; as much as thirty litres, or nearly twice as many imperial pints, was in one instance drunk, with proportionate diuresis, in twenty-four hours. The symptoms usually began on the day of the accident, but were in one case delayed until the sixth day afterwards. In three cases the disorder subsided after some weeks; in the fourth it lasted six years, coming to an end after an attack of small-pox.

A blow on the head bruises the brain, if anywhere, most at the spot diametrically opposite to where it fell—acting by *contrecoup* as it is termed, the result of which is better known than the manner. In these cases, therefore, of frontal injury, the hinder part of the encephalon was chiefly endangered; and it is possible that the bruising or interstitial hæmorrhage, which we should expect from such accidents, may have involved the medullary region of experimental polyuria. This list might be considerably increased.

A girl of fourteen fell from a height upon her feet[1] with consequent 'head-symptoms,' among which was hæmorrhage from the left ear, indicative of fracture of the base of the skull. On the ninth day she became polyuric, and ceased to be so on the fifteenth. She drank six litres or about ten imperial pints a day, and passed water proportionately.

In all these instances the urine was without sugar; many cases are to be found in which in similar circumstances the urine has become both excessive and more or less saccharine. And both these classes bear a near resemblance, both in the nature of the accidents so followed and in the usual transience of the urinary change, to the examples of traumatic glycosuria related elsewhere (page 81).

The change, however, whichever it be, is not always transient; Mosler mentions a boy of seventeen who fell upon his head at the age of three, and had been polyuric ever since.

[1] 'Treatise on Polyuria,' by Lancereaux, p. 14.

From traumatic polyuria we may pass to polyuria dependent on obvious and recognisable disease of the brain.

Consequent upon disease of the brain or membranes.

I may relate an instance within my own experience.

Diabetes insipidus in a child consequent upon tubercular disease of membranes at the base of the brain.

Mary Cragg, 5 years old, coming on her mother's side of a highly consumptive family, was admitted under my care in the Hospital for Sick Children, on June 7, 1867.

A year previously she was observed to suffer from excessive thirst, and at the same time her urine became extravagant in amount, so that at night she had to be continually getting out of bed. She lost flesh for a time, though she kept her appetite; after six months, however, she had more than regained her loss, aided possibly by a course of rum and milk which had been prescribed for her.

On her admission, her urine, which was almost like water, averaged, according to her mother's statement, about 10 pints in the twenty-four hours, but during her stay in the hospital it never exceeded 94 ounces. It varied in specific gravity from 1,008 to 1,003.

She was well made and well nourished, with a rosy complexion, blue eyes, and light brown hair. She had occasional headache, but no signs of pulmonary disease. She was restless and habitually thirsty. The tongue was moist and pale, the skin warm and dry, the bowels generally confined. She sometimes vomited after eating or drinking. The urine gave no trace of sugar or albumen, nor any abnormal appearances under the microscope, unless a few cells of apparently renal epithelium could be so regarded. Her temperature, which at first had been natural, gradually increased to 102·8 in the morning, 104·0 at night, and simultaneously with the rise of temperature her pulse increased to 180, her headache became more constant, and herself drowsy, often asleep, and yawning when awake. The drowsiness then so far approached coma that the urine was passed involuntarily, and in this state she was taken out by her parents on June 8, five days after the access of fever drowsiness and increasing headache had led to the belief that she was the victim of tubercular meningitis.

She died two days afterwards, not latterly drowsy, but wakeful and given to walking about restlessly.

Dr. Reginald Stocker, then registrar to the hospital, obtained leave to examine the body. At the base of the brain, about the posterior perforated space, the crura cerebri, the Sylvian fissure, and the upper surface of the cerebellum, the pia mater was studded with miliary tubercles and thickened with inflammatory deposit. There was similar thickening at the upper part of the longitudinal fissure. The membranes were generally injected, and the subarachnoid fluid increased, as also was the ventricular fluid; this only however to the amount of about an ounce and a half of clear liquid, not enough to cause flattening of the convolutions. The choroid plexuses were vascular, and the cerebral veins turgid, but the brain substance was generally natural in appearance. No bulky masses of tubercle were found. The membranous inflammation, though partially recent, had evidently been preceded by a similar change of older date.

The fourth ventricle was somewhat distended, but gave no other evidence of alteration to the naked eye. No microscopic examination was made.

The kidneys were congested, spotted on their surfaces with injection; in other respects they appeared natural.

No tubercle existed elsewhere than in the brain. The lungs were natural, and the only peculiarity discovered beyond what has been mentioned was enormous flatulent distention of the stomach. It must be stated that the post-mortem was not procured until two days after death.

As usual in such cases, the kidneys were here simply hyperæmic; if their change of function depended on structural disease, it was at any rate external to themselves. It could but be attributed to the intracranial tuberculosis.

The position to which the tubercular disease was limited was such that it must have been in immediate contact with the edges of the fourth ventricle, and it is probable that the symptom was determined by irritation here, possibly of the trunks of the vagi; or by a similar influence upon the upper surface of the cerebellum, which also has been shown capable of giving rise to the urinary change. The membranous thickening was of sufficiently old date to be credited with the polyuria, though recent

inflammation also existed. Looking at this case and others like it, one is inclined to wonder not that polyuria should result from such a cause, but that it should not occur more often.

Sir Thomas Watson[1] saw a marked instance of this disease, or chronic diuresis as he prefers to term it, which had apparently a similar origin. A boy passed about ten pints a day of dilute urine which had a specific gravity of 1,002 or lower. He was proportionately thirsty, and when debarred from drink gained weight by absorption, as was supposed, of moisture from the atmosphere. His disorder, which was unmitigated by treatment, lasted three years. He died at the age of thirteen. 'After death scrofulous tubercles were found in his brain, and in his lungs. His kidneys were gorged with venous blood, but of healthy structure. There was nothing wrong apparently in his organs of digestion.'

The following case occurred in the practice of Dr. W. Roberts:[2]—

A lad of 16, a warehouse clerk, became thin and weak; he drank much, never perspired, and suffered from dyspeptic symptoms, flatulence and occasional vomiting, with want of appetite. He became exceedingly emaciated, the tongue glazed, and the skin dry. He had intense and incessant thirst, and passed water which, until near the end of his illness ranged from 9 to 14 pints a day. What he drank was found on measurement almost precisely to equal what he voided as urine. This secretion contained neither albumen nor sugar; in specific gravity it varied from 1,002·7 to 1,004, and gave a daily total of from 394 to 505 grains of urea, which, considering that his weight was but 78 pounds, and his normal yield of urea estimated at 275 grains, was a considerable increase.

The debility and loss of flesh increased with little variation, until he was suddenly seized with convulsions and insensibility. These were succeeded by a condition of semi coma, which lasted three days and then passed off, leaving the patient much as he

[1] 'Lectures on the Principles and Practice of Physic,' 4th edit. vol. ii. p. 665.

[2] 'Roberts on Urinary and Renal Diseases,' 2nd edit. p. 204.

was before the seizure. During the coma the diuresis diminished, but it increased again with his returning consciousness. After an interval of ten days, the convulsions and insensibility recurred and proved fatal. He died five months after the weakness, thirst, and wasting had marked the beginning of his illness; thirteen days after the first fit.

'A nodule of yellow tubercle of the size of a hazel nut lay imbedded in the left hemisphere of the brain, in the border of the longitudinal fissure, midway between its extremities, and cropping out on the surface. Another nodule as large as a garden bean was found in the posterior border of the right half of the cerebellum. The floor of the fourth ventricle was especially examined; it was pale and natural, with no tubercular mass in its immediate vicinity. The brain was superficially spotted with vascularity, but the membranes were free from tubercle, and otherwise healthy. There was an excess of clear fluid in the ventricles and in the subarachnoid space.

'The kidneys were voluminous, smooth, flaccid, and the two together weighed 8 ounces. On section they showed no disproportion between the pyramidal and cortical portions, nor any other morbid change. Examined microscopically the tubes and cells appeared normal.'

There was extensive tubercular disease with vomicæ in the lungs, and tubercular ulceration of the bowels.

In this case the symptoms were obviously dependent in part upon the tubercular disease of the lungs and bowels.

Meningitis unconnected with tubercle is also a possible cause, as also are intracranial growths of many types.

The epidemic[1] cerebro-spinal meningitis has also been known to be thus succeeded. A boy of the age of seven had polyuria which was traced to his sharing in an epidemic of this nature when a year old.

As an example of the origin of the disease in an intracranial growth other than tubercle, I may cite the following:—

A young woman twenty-two years of age, who had had

[1] Reported by Mosler, 'Virchow's Archives,' vol. lxviii. part 1.

fits in infancy, suffered from pain in the head, and vomiting with the characteristic symptoms of diabetes insipidus. The urine contained no sugar. At the post-mortem which was made by Virchow[1] a gliomatous tumour, 5 centimetres long, 1 in thickness, was found adhering to the floor of the 4th ventricle, and partially filling the cavity reaching from the aqueduct of Sylvius to the nib of the calamus scriptorius.

The same author relates an instance of the urinary change, as consequent upon syphilitic disease of the brain, with softening of the left cerebral hemisphere, pons, and medulla.

Many instances have been recorded, in which, though the disorder has not ended fatally, or there has been no post-mortem examination, yet the concurrence of the urinary change with disease within the skull has been placed beyond doubt by the presence, not singly, of otorrhœa, hemiplegia, squinting, amaurosis, or epileptiform convulsion.

Insipid and mellitic diabetes sometimes replace each other.

The following case occurred in the practice of Trousseau: it is of interest as showing the pathological alliance of insipid and saccharine diabetes. The one state was exchanged for the other; and the morbid changes both in the lungs, and in the medulla, so far as M. Luys' observation extended, are such as are common to both. M. Luys has decribed precisely the same nervous changes in the ordinary saccharine form; and it can scarcely be doubted that had he examined hardened sections, he would have found the peculiar signs of perivascular destruction which that method, as I have shown, never fails to display in connection with the sugar-yielding disease.

A man 35 years old, who, five years before, had been the subject of saccharine diabetes, was admitted into the Hôtel Dieu with simple polyuria, passing from 6 to 7 litres of urine daily without either albumen or sugar, and of a specific gravity between 1,001 and 1,007. It does not appear at what epoch the

[1] Mosler, 'Virchow's Archives,' vol. xliii. p. 225.

sugar withdrew from the urine. He had become phthisical, having numerous and large cavities in the lungs. Being attacked with acute pulmonary symptoms, the urine fell to a small amount. The phthisis advanced rapidly, and he fell into a scorbutic state, with an outbreak of purpura. Fourteen days after these symptoms he sank without having presented any cerebral symptoms.

M. Luys found after death that the anterior wall of the fourth ventricle was unnaturally vascular, streaked with considerable vessels, and mottled with tawny patches.

Transverse section showed the grey matter injected even to a roseate hue, while the nerve cells within the discoloured patches were in an extreme state of fatty degeneration.[1]

Intra-cranial sources of the disease vary more in kind than in position.

So far it has been shown that the intracranial sources of diabetes insipidus, though various in kind are constant in position. Where the position has been exposed after death, it has always involved the medulla or cerebellum. And where the locality was a matter of inference only, as in many instances of temporary polyuria from injuries, the basal and hinder parts of the encephalon have mostly been those obviously imperilled.

In kind there is a wide, almost an unlimited, range. The bruising or punctiform extravasation, such as we know to be caused in the brain by external violence, must, if we may judge of those brains which have not been examined by others which have been, be regarded sufficient to the incitement of polyuria, which, when thus caused, seldom lasts long. Meningitis, whether tubercular or epidemic, or the adhesions which meningitis has left, are sufficient without any recognisable change below the surface. Deeper, the symptoms may depend upon tubercles or other growths; softening in connection with syphilitic disease; and changes consequent upon disease of the temporal bone.

Lastly, like diabetes mellitus, the disorder may depend

[1] The clinical aspects of this case are fully reported in the 'Gazette Hebdomadaire' for 1866, p. 181. The morbid appearances in the 'Gazette des Hôpitaux' for 1861, p. 261.

upon minute changes evident with the microscope, though scarcely so to the naked eye.

Possible origin in abdominal disease.

Some instances would seem to show that the disease may take its rise in irritation or compression, by means of an abdominal tumour of nerves leading to the kidney. Hydruria may be experimentally produced, either by section of the splanchnic nerves, or by irritation of the pneumogastric. Possibly the following cases are to be explained by one of these modes, or at least by an influence upon neighbouring nerves, whether of an irritative or paralysing kind.

Professor Haughton [1] tells us of a woman who died with characteristic symptoms of diabetes insipidus, together with constipation and abdominal swelling, all of which had commenced simultaneously nine years before.

'The large intestine was immensely distended with accumulated fœcal matter; while above the ileo-cæcal valve, the small intestines, for a considerable distance, were filled with gas—accounting for the alternate clearness and dulness, on percussion, of parts of the abdomen during life.

'The obstruction was caused by a tumour, the size of an orange, situated between the back of the uterus and the front wall of the rectum; connected to each of these parts by fibrous bands and pressing firmly on the latter. The tumour cut like india-rubber; its section was white and firm, with gritty particles through it. The mesenteric glands connected with the colon were enlarged and hardened, having the shape, size, and colour of cherry-stones.'

The kidneys were uneven and cysted; the heart large apparently from renal hypertrophy; the brain was only imperfectly examined, but presented no obvious anomaly.

The growth was apparently a fibrous tumour of the uterus. The mesenteric glands were probably affected

[1] 'Dublin Quarterly Journal' for November 1863, p. 323.

only secondarily to the accumulation in the colon. It is easy to suppose that the extreme distention of the large bowel may have caused, by extension or pressure, some such nervous injury as to have set up the hydruria, of which the facts, so far as they are related, suggest no other explanation.

State of urinary organs.

The organ which in relation to diabetes insipidus stands next to the brain, that which is the instrument of hydruria, as the liver is the instrument of glycosuria, is the kidney. The only constant changes which have been found in this gland show exaggerated action rather than altered structure. The kidneys are usually hyperæmic; injection of the malpighian bodies has been especially observed, and as in the instance in my own experience, punctiform injection of the cortical tissue. The glands, except in the later stages of the disease, are increased in bulk and weight.

Later atrophic or inflammatory changes may be induced, apparently by the accumulation or incomplete escape of the superabundant urine.

Sacculation of kidney probably the result, not the cause, of the polyuria.

The bladder, ureters, and pelvis become dilated, and the kidneys sacculated to the destruction of their secreting structure.

Dr. Eade describes the post-mortem appearances[1] in a man, who sank at the age of 65, 'from the exhausting effects of the disease with its continued diuresis, and the frequent urgent calls, both by day and night, to empty the bladder.' Beyond injection of the lining of the stomach, no morbid appearances were found save in the urinary tract, and such as must have been caused by distention. The bladder was enlarged, thickened, and fasciculated internally. The ureters were dilated, in places to the size of the little finger. The infundibula and pelvis were dilated, and the sacculated kidney in process of establishment. The organs were pale and flaccid, as if undergoing absorption, the cones being so much denser

[1] 'Beale's Archives,' vol. ii. p. 8.

than the cortex that they could be felt through it as separate nodules.

The brain was not examined.

The same writer describes the state of the organs after death,[1] in a man who died in a condition of typhoid prostration, having had the disorder for twenty years. The bladder, ureters, and kidneys were dilated; a representation of one of the latter shows it as a partitioned bag with walls as yet thickly composed of renal structure—in a condition, that is, of marked, though not extreme distensive sacculation. Dr. Beale, who examined the kidneys microscopically, found some of the tubes narrow and wasted, others of more than twice their natural diameter; the perivascular fibroid tissue was increased, the malpighian bodies were small, the epithelial cells were irregularly multiplied, and the changes, in short, were such as are usually found in kidneys which have been subjected to the pressure of retained urine.

The results of urinary accumulation were further advanced in a case recorded by Dr. Strange.[2] A boy died at the age of 18, having had diuresis to the extent of about 12 pints a day for a number of years. His death was preceded by drowsiness, headache, convulsions, and coma, apparently of uræmic origin, which symptoms had supervened upon restriction of drink. The bladder was pyriform in shape, as in childhood, reaching upwards into the abdominal cavity. Its walls were thickened. The ureters were dilated to the circumference of from 3 to $4\frac{1}{4}$ inches; the right was at first mistaken for the ascending colon. The kidneys were expanded to mere sacs of from twice to thrice the extent of the healthy organ; no secreting substance either of cones or cortex could be found; the sacs were 'divided into a number of cells by the intertubular septa which occur in the fœtal state.' The walls and septa were formed of fibrous tissue, and lined with what looked like serous membrane. Dr.

[1] 'Beale's Archives,' vol. iii. p. 128.
[2] *Ibid.* p. 278.

Strange inclines to the belief, after discussing both views, that the condition of dilatation he thus describes was congenital rather than acquired. But the accuracy of his description allows us to view the case, so to speak, with our own eyes, and does not permit us to doubt that the expansion and atrophy were alike brought about by urinary pressure; it seems impossible, indeed, that the stretching jointly of the bladder and ureters, with the equally characteristic state of the kidneys, could have originated in any other way; the only uncertainty would seem to be whether the repletion of the urinary cavities was due to excessive secretion, or to an impediment in exit no longer present when the body was examined.

In the absence of stricture or other hindrance to the outflow of urine in these cases—and others like them might be cited—it is clear that the stretching of the urinary cavities has been due to excessive secretion. The urine has been poured into them faster than convenience allowed of its discharge. Whether emptied too slowly or filled too fast, the habitual repletion is the same, with its necessary results in dilatation and glandular atrophy. Thus the sacculation is a consequence of the disorder, and not its cause. I have seen a lesser degree of the same change with diabetes mellitus; though in this disorder the diuresis, if so profuse, is never so long continued. It is to be noted that sacculation of the kidney does not of itself cause diuresis.

Scattered suppuration in kidneys.

Similarly engendered, other renal changes may ensue as secondary to the diuresis. The kidneys may become the seat of that scattered suppuration which is a frequent associate of sacculation and perhaps almost the natural ending of stricture.

A man of the age of 50 [1] died with diabetes insipidus, of which the only peculiarity was, that for the last three months he had febrile symptoms, with nausea, loss of appetite, and epigastric tenderness. The urine usually

[1] Related by M. J. Mascarel, 'Gazette des Hôpitaux,' 1861, p. 90.

amounted to about 6 litres a day, and contained neither sugar nor albumen. With the febrile symptoms the urine acquired a slight yellowish white puriform deposit, which two days before death became evidently purulent.

The post-mortem observations were negative, save as touching the urinary organs; the head was not opened; the bladder was hypertrophied; the pelves and ureters contained creamy fluid; the left kidney was swollen, and in its cortex were 8 or 10 abscesses varying in size from a pin's head to a small filbert, the smaller containing concrete, the larger fluid pus. The right kidney was injected, especially the cones, from which could be squeezed creamy fluid, such as was found in the pelvis. It contained no abscesses.

The condition thus described was clearly that form of disseminated suppuration which I have elsewhere described as uriseptic, and shown to depend on the resorption by the kidney of decomposing and generally purulent urine. It is probably consequent on accumulation and putrefaction of urine, and has no further association with diabetes insipidus than as a possible consequence of the distention and imperfect emptying of the urinary cavities which the disease may entail. The febrile symptoms which probably marked the beginning of the suppurative process, did not set in until after many months of the diuresis, and therefore could have had nothing to do with its causation, and indeed, this inflammatory affection usually diminishes, instead of increasing, the urine. The deficient acidity of the urine of diabetes insipidus, and its consequent proneness to putrefaction, must make it the more apt to give rise to this disorder, of which the source is septic.

Death sometimes due to secondary renal changes.

These secondary conditions sometimes bring about the mortal ending of the disorder; the destruction of the kidney by sacculation having been succeeded by uræmia; the disseminated suppuration by the febrile pseudo-typhoid state which is the expression of the systemic contamination it involves.

We may accept the conclusion that beyond mere hyperæmia, all the renal changes coincident with diabetes insipidus are consequent upon it, not antecedent to it.

Other organs scarcely need mention, as what could be said of them would be but negative. Where the disease has been dependent upon encephalic tubercle, tubercle has been found in other organs, naturally with much frequency in the lungs; but there seems to be no tendency in the disease to cause tubercle, or to set up the peculiar pulmonary disorganisation of diabetes mellitus.

Summary of pathology.

Thus morbid anatomy displays what physiology had shown to be possible; the abnormal diuresis which constitutes the disease is not due to structural change of the kidney, or to irritation arising within itself, but to an influence reaching it from without, travelling presumably by the nerves, and having its origin—at least so it has proved wherever it has been traced—in the cerebello-medullary region. The nature of the central change is various; it may be such injury of nerve tissue as results from concussion; it may be tubercle or other growth; it may be old false membrane, whether originating or not in tubercular disease; and it possibly may be such intimate disorganisation as has been shown to be constantly connected with diabetes mellitus.

Subjects.

Age.

Diabetes insipidus is a disease especially of infancy and childhood. It has been found immediately after birth.

Under the age of 5 or 6 it occurs almost to the exclusion of the saccharine form; afterwards up to advanced life either may happen, the insipid preferring the earlier, the mellitic the later years.

Dr. Roberts,[1] with his usual industry, has tabulated the age at invasion in 70 cases.

His results are as follows:—

[1] I am glad to acknowledge the assistance I have had in treating of this subject from the painstaking and compendious account Dr. Roberts has given in his work on Renal and Urinary Diseases.

The disease begun in infancy	.	.	in 7 cases	
,, ,,	from 5 to 10	years in	15	,,
,, ,,	,, 10 to 20	,,	13	,,
,, ,,	,, 20 to 30	,,	16	,,
,, ,,	,, 30 to 50	,,	15	,,
,, ,,	,, 50 to 70	,,	4	,,
			70	

Lancereaux,[1] who collected 21 cases, found 9 between the ages of 5 and 20; 8 from 21 to 40; 4 above 40.

I have elsewhere referred to instances in my own practice where the disorder commenced respectively at the ages of 12 months; 2½, 4, 8, and 60 years.

Sex. As to sex, taking cases of all ages, this disease, like diabetes mellitus, preponderates in the male.

Of 77 cases collected by Dr. Roberts, the subjects were male in 55, female in 22. Of Lancereaux's 21, 14 were male, 7 female.

Thus taking all ages together, diabetes insipidus, like the saccharine form, occurs at least twice as often in the male as in the female. Probably, however, the inequality is not so great, and possibly not existent in childhood. Of the four children I have mentioned as patients of my own, only one was a boy.

Causes.

The etiology of the disease is to a certain extent comprised in its pathology; I need, therefore, say no more as to the origin of the disease in obvious lesions of the brain or elsewhere, or in accidents calculated to produce them. Many circumstances, however, present themselves as antecedent to the disorder, of which morbid anatomy can take no count since their essential lesion has not been exposed to view. Hereditary influence, fits of drunkenness, mental emotion, violent muscular efforts, syphilis, and attacks of febrile disease, are among the more certain

[1] Lancereaux has written an excellent treatise on the disease to which every one interested in the subject cannot but stand indebted.

of these; exposure to cold or to the sun, and blows upon the loins or right hypochondrium stand in a more doubtful relation. And a large number of cases occur—perhaps a majority—in which it is impossible to form any reasonable conjecture as to the source of the disease.

Lancereaux gives the following table, acknowledging at the same time his debt to Roberts, who had previously compiled one which, from a smaller number of instances, gave very similar results. He examined 72 cases; the cause was hypothetically traced in 51, undiscoverable in 21.

Circumstances to which the Polyuria was traced.

Injuries of the head	5	cases
Contusions affecting other parts of the body, or violent efforts	3	,,
Non-traumatic lesions of the encephalon	7	,,
Hysterical and nervous conditions	7	,,
Mental emotion	2	,,
From habitual alcoholic excess, or succeeding immediately upon intoxication	7	,,
Sudden chills	3	,,
Sun-stroke	1	,,
Acute inflammatory or febrile disorders	5	,,
Hereditary influence	11	,,
	51	
Instances in which the polyuria could not be traced to its cause	21	

It is possible that some of these supposed causes may be no more than chance antecedents; as to others there seems less room for doubt.

Among the indubitable, hereditary influence may be first mentioned. Lancereaux has collected a considerable number of instances in which subjects of this disease have had relatives affected similarly or with diabetes mellitus. Hereditary tendency.

In several cases many members of the same family—in one three brothers and a sister, their uncle and some of the uncle's children—in another, two brothers, two sisters, and their mother—had polydipsia dependent as far as was known upon diabetes insipidus. In other instances both kinds of diabetes concurred. Trousseau tells us of a young woman with insipid diabetes whose grandfather had the mellitic; and indeed the tendency of diabetes insipidus to

occur in families where the saccharine form has shown itself, seems even more marked than that of the former kind to multiply by consanguinity.

Drunkenness.

Perhaps among the causes of the disease irrespective of race none is more definite than drunkenness; and generally after the same manner; it must be acute, and the subject of it, to use the distinction of the learned Scot, not *ebriolus* but *ebrius*. A person gets what is vulgarly termed dead drunk; on recovering consciousness he is polyuric and so remains.

A patient whose case is related by Professor Haughton of Dublin,[1] 'attributed the commencement of *the thirst* to a carouse on Lager beer and brandy, in New York, during the hot weather; on the morning following his debauch an intolerable thirst had seized him from which he had never subsequently been free.' In its mode of origin this instance seems typical; it must be mentioned, however, as introducing an element of doubt, that the man had tertiary syphilis.

It is highly probable that in such cases minute extravasations of blood have occurred consequently upon the congestion of drunkenness which have acted on the irritative centres of the disease.

There are several instances in which hysterical or neuralgic persons have been attacked; but we may believe that something beyond the general state of system characterised by these terms is needed to establish the disorder in a permanent form.

Mental emotion.

Mental emotion, as with diabetes mellitus, has been credited, probably justly, with its creation.

A woman 32 years of age,[2] who was abruptly apprised of the death of her husband, was thereupon seized with pain in the head, without convulsions or loss of consciousness, heat of skin, and inextinguishable thirst. She drank a pail of water that night, passed a proportionate amount of urine, and remained polyuric; the condition, however,

[1] 'Dublin Quarterly Journal' for November 1863, p. 321.

[2] Cited by Lancereaux, p. 22.

once intermitted during a febrile attack at a menstrual period and returned with its cessation. The urine ranged in quantity from 5 to 15 litres; in specific gravity from 1,001 to 1,005.

Strains and muscular efforts.

Violent strains and muscular efforts have been so immediately followed by the disorder that we cannot choose but attribute it to injury they have wrought.

Dr. Roberts has quoted two well-marked instances—one from P. Frank.

A boy of 12 strained himself in pushing a cart wheel sunk in the mud; he became immediately polyuric, and ultimately died, as was supposed, of an over dose of nitre given for its relief. The second occurred in the practice of Professor Gregory at the Edinburgh Infirmary. A girl of 19 when going down a flight of steps slipped, but with great exertion saved herself from falling. Immediately afterwards menorrhagia began, and on the same evening inordinate thirst and diuresis. The hæmorrhage subsided under alum, but the diuresis continued, the urine amounting to 50, 60, and on one occasion to 72 pounds in the 24 hours. Under lime water and galls it gradually fell to from 5 to 10 pounds, and she left the hospital in good health, excepting as regards this secretion.

It is possible with mental or bodily shocks, as with drunkenness, that the *fons et origo* may be cerebral extravasation.

Cold.

Many instances are related in which the characteristic thirst and diuresis have been attributed to the drinking of cold water or to cold otherwise applied.

An old man drank a glass of wine and water in hot weather while perspiring; he at once was stricken with unquenchable thirst, and ultimately died with marked symptoms of diabetes insipidus.

A boy of 14 [1] while sweating drank very cold water from a spring, and became thereupon polydipsic. And cases of the same sort might be multiplied; with such in view,

[1] Cited by Lancereaux, p. 25 and 26.

everyone must regard himself fortunate who escapes the same fate, for all must have incurred the risk.

As with diabetes mellitus which has been similarly attributed, it may be asked, whether untimely or inordinate drinking does more than draw attention to the disease or mark its commencement.

Perhaps there is less improbability in the supposed origin of the disorder in external cold, though even here the evidence is scarcely conclusive.

A man got his feet wet in cutting rice early in October; the same evening he became polyuric.[1]

An advocate found himself in the same state after having fallen into a river while hunting.

Syphilis.

Syphilis appears in certain cases to have been something more than an accidental complication of the disorder. It has been found in connection with it in many cases. Syphilitic changes in the skull or its contents are undoubtedly competent to cause either saccharinity or mere increase of urine; a case in point has been related by Mosler, in which polyuria in a syphilitic subject was associated with convulsions and hemiplegia, and at last found to depend on softening of the left cerebral hemisphere, medulla, and pons.

Inflammatory or febrile disease.

Lastly, among the circumstances in which polyuria has taken rise, must be mentioned acute disease of the inflammatory or febrile type. It has thus succeeded upon diphtheria, enteritis, small-pox, acute rheumatism, and ague; sometimes beginning during convalescence with marked cephalalgia.

SYMPTOMS AND COURSE.

The chief, and sometimes the only, symptoms of diabetes insipidus are diuresis and thirst. The patient may, with little disturbance of health, make more water and drink more than in any but the most severe and

[1] Quoted by Lancereaux, loc. cit.

destructive forms of diabetes mellitus. But the thirst of the insipid form is perhaps the less tormenting; it is to be quenched by a sufficiency of drink, and this supplied, the patient is at ease. With the mellitic, the drought is only mitigated by potation. The thirst of mere polyuria is to be cured by drinking; the thirst of glycosuria only by diet.

Thirst.

Debarred from other liquids polyuric patients frequently drink their own urine; I had two who did so. This act is almost pathognomic. Water makes its exit from the body much as it went in; sometimes with a specific gravity under 1,002; acquiring in its passage no more extraneous matter than is often found in the product of a mineral spring, and capable of quenching thirst, however open to æsthetic objection.

Health may be little disturbed if drink be not restricted.

With drink unrestricted, the tongue in diabetes insipidus may remain moist, the skin soft, smooth, and capable of perspiration, the bowels sufficiently active and none of the functions of body or mind be obviously deranged. The disorder does not necessarily involve much more than loss of water, which can be easily supplied; while with its saccharine congener there is loss of water and of solids, and the development of a blood poison in the shape of the superabounding sugar. Diabetes insipidus therefore would seem to be the less threatening, and indeed is in its simplest form by far the less formidable disease. But though not in itself quickly fatal, it may be the result of lesions that are so. It has been shown to depend upon tubercular disease of the brain, or upon extensive softening connected with syphilitic disease, which conditions will proceed to their natural issue, notwithstanding that they may have been more or less masked by the prominent urinary disturbance.

Course varies with cause.

According to the nature of the primary lesion, recovery or death may ensue quickly or slowly; the traumatic cases are mostly finished one way or the other in a few weeks or months, though in some instances years have elapsed and effaced all other traces of the injury,

but left the polyuria; from drunkenness the disorder runs, so far as we may judge from marked instances, a severe course, sometimes ending fatally within a few months; one thus terminated in two months.

If the disorder be hereditary or apparently spontaneous, in which case the central change would seem, however persistent, to be, save as regards the polyuria, often without result, the symptom may last indefinitely, or at least until after long years it has caused such distention of the urinary receptacles that the kidney is destroyed by sacculation, and death by uræmia results. This issue, though perhaps to be regarded as the natural conclusion, may be very remote.

Dr. Strange's case, already related, proved fatal in this way, at the age of 18. The diuresis had existed for 'a number of years.' In this instance the course was comparatively speedy.

May last indefinitely.

In its simplest form, or with the minimum of organic change which is capable of causing it, the disorder may persist from youth to age, and wear the aspect rather of a troublesome propensity than of a disease tending to a fatal issue.

Instances of polyuria profuse and long continued.

An extraordinary consumption of water was discovered in a humble French household, and traced to a child of three years old, recently come home from nurse, who, from her birth, had been afflicted with 'a drought beyond example.' She drank every day nearly two pails of water, and was eventually driven from home by the ill-treatment she received in consequence of this expensive habit.

When she was 22, a cobbler, unaware of her propensity, married her; he found that his earnings did not suffice to keep her in water, insomuch that he was fain to collect and liquify snow and ice for her use. She drank 4 pails a day, of which the price was 12 sous. She made him the father of eleven children. When she was 40 years old, she was examined by a scientific commission, and drank in the presence of its members 14 quarts of water

within ten hours, and voided 10 quarts of nearly colourless urine.

She had fair health so long as she could drink freely. She drank most when pregnant, least when out of health. She was abnormally sensitive to alcohol. The urine, which was in proportion to what she drank, was fœtid. The disorder was not hereditary, nor could any cause be assigned for it beyond the fact that, in her infancy, her grandmother had been in the habit of giving her wine.[1]

In the same paper is recorded the case of a farm labourer, who drank as deeply of 'allaying Thames.' When made the subject of report he was 51 years old. His thirst had come on 24 years previously after a prolonged attack of ague and fever. He usually drank a quart of water at a time, and repeated the draught 16 or 18 times in the day and night. He passed about as much urine as he drank water. In one night under observation he passed between 5 and 6 quarts of urine without sediment. He was in good general heath, and equal to severe farm labour, threshing, and mowing.

An artisan,[2] 55 years of age, admitted into the Hôtel Dieu for a bruise of the knee, had had constant thirst, with commensurate diuresis, since he was 5 years of age. From the age of 16 he had drunk not less than two bucketfuls of water daily. While in the Hôtel Dieu he drank on an average 32 pints of water every day, often swallowing two quarts at a draught. Yet he looked and seemed well; had the strength proper to his size and age; was the father of several children, and suffered no inconvenience save from the necessity of drinking and voiding his urine so frequently.

These cases show the disease in its most protracted form; they at least prove that the *urinæ profluxio* is not of itself very harmful. When death comes within a few

[1] This patient was last seen in the year 1791. The case is given with apparently truthful detail in 'Medical Facts and Observations,' vol. ii.

[2] Cited by Dr. Willis from M. Boissat. 'Willis on Urinary Diseases,' 1838, p. 3.

months, or even weeks, of the access of the symptom—of which there are examples—it has probably been directly due to the lesion in which it has originated.

Outset sometimes sudden.

It has often been noted that the disorder has been sudden in its commencement; cases have been already related in which the symptoms have begun in full force immediately after the debauch or other circumstance in which they arose—a mode of access suggestive of hæmorrhage, possibly minute or punctiform, within the nervous centres.

Less threatening than saccharine diabetes.

With regard to the progress and complications of the disease, there is little more to be said. Trousseau speaks gravely of its results, and regards phthisis as one of them. But it is probable that this is rather the sequel of a primary tuberculosis than of the polyuria. Polyuria of non-tubercular origin appears to have no such tendency as saccharine diabetes has to simple pulmonary caseation.

Diarrhœa.

Patients are prone to diarrhœa. They are especially sensitive to cold, under which they become pinched and blue, and pass water with exaggerated profusion. The bodily temperature in this disease, unlike what happens in diabetes mellitus, is but little lowered. The habitual range has been in the cases I have seen from 97 to 99.

Temperature.

Appetite.

The appetite is sometimes excessive, not always so, late in the disease its failure may be of evil omen. A patient of Trousseau's, who dined at a restaurant where bread ad libitum was included in the charge, was paid by the proprietor to dine elsewhere. In the cases I have seen the appetite has not been unnaturally great.

Epigastric pain, dryness of the tongue, and much general distress is produced by enforced abstinence from water.

Occasional tolerance of alcohol.

A tolerance of alcoholic drinks appears to be sometimes established, as with diabetes mellitus. A man mentioned by Trousseau on several occasions, drank for a wager 20 bottles of wine without any effect on the nervous system. The reverse conditions however, one

of increased susceptibility to intoxicating liquors, has been noted (page 203).

Œdema.

In some instances purpura has occurred, in others œdema, but these are rare results of the anæmia to which the disease tends. In a case to be subsequently related (Percy Russell) small boils and impetiginous spots appeared; but the furuncular disposition is not marked as with diabetes mellitus. Retinal hæmorrhage[1] has been found in connection with the disease at least in one instance.

Boils.

Sometimes modified by intercurrent diseases.

Diabetes insipidus is sometimes remarkably influenced by intercurrent disease, and even by the progress and termination of pregnancy. A[2] young man had thirst and diuresis up to the age of 18; he then had pleurisy, and a blister which suppurated for 25 days; when the blister healed, he found that he had lost both pleurisy and polyuria. In another instance[3] the urinary disorder, which had lasted for 18 years, came to an end after an attack of acute rheumatism, which had been treated with nitrate of potash. Febrile disease, however, does not necessarily affect the complaint, for in one of my cases (Percy Russell, p. 221) a sharp attack of scarlatina not only left it as it found it, but scarcely modified it even at the height of the pyrexia.

Pregnancy.

With regard to pregnancy, Dr. Hughes Bennett mentions an instance in which a woman became polydipsic without apparent cause in the fifth month of pregnancy, and ceased to be so two days after delivery. In other instances, the whole process of child-bearing has been accomplished[4] with no modification of the disorder.

In the ordinary course of the disease the generative faculties are unimpaired, the intellect clear and the temper equable as in health, though restriction in drink may

[1] Galezowski, 'Étude ophthalmoscopique sur les altérations du nerf optique, &c.'

[2] Cited by Willis, 'Urinary Diseases,' p. 4.

[3] Cited by Roberts.

[4] See case reported by Dr. Matthews Duncan, 'Obstetrical Journal,' July 1874, p. 220.

Enforced restriction one of the dangers of the disease.

render it morbidly fretful or passionate. From this cause patients suffer not only in comfort but in appearance and in health even to risk of life. Without mischievous interference, save that the subject of the disease is a valetudinarian, it is hard to fix upon any function necessarily disturbed, except it be that at last the kidney may be incapacitated by distention, and uræmia close the scene.

May end in uræmia.

The detailed cases which follow may help to remedy the incompleteness of this sketch of the symptoms of a somewhat rare disease. And to these also I must refer for many particulars with regard to the urine, and its bulk relatively to the drink.

URINE.

Urine sometimes exceeds drink.

Usually in this disorder the fluid introduced into the stomach slightly—and but slightly—outmeasures that which escapes by the kidneys. In a severe attack, however, as in that of Cox (page 213), careful and repeated observations may prove the urine habitually to exceed by a little the volume of the liquids swallowed. Water has either been made in the body as Lavoisier supposed, or else, what is more probable, the excess is in part due to the aqueous constituent of solid food, and perhaps in larger part to absorption from the atmosphere. I satisfied myself that, as has been related in other similar instances, my patient Cox gained weight without eating or drinking (page 213), which can only be explained, as far as I see, by the absorption of atmospheric moisture.

Super-aqueous.

The leading peculiarity of the urine is excess of water. It has a specific gravity which usually ranges between 1,006 and 1,002. In the instance of Botting (page 218) it once descended to the exceptional depression of 1,001·7, the minimum of my own experience. It is generally feebly acid or nearly neutral. It is clear and bright when passed and seen in bulk has a greenish tint like that of the stone *aqua marina*. It rapidly becomes ammoniacal,

acquires a fishy smell, and becomes turbid with earthy phosphates.

With regard to its natural constituents the amount of the urine as a rule more than makes up for its poverty. This holds strikingly with urea which in ordinary instances, in which the kidney is not as yet seriously injured by distention, is excreted in thrice or four times the normal quantity. Cox (page 215), who weighed under 2 stone, passed under ordinary mixed diet an amount of urea which varied from 11 to 26 grammes; her normal amount probably being under 6. Botting, a younger child of about the same weight, passed under similar diet from 9 to 23 grammes. And Russell passed apparently nearly as great an excess, though from the impossibility of collecting all the urine it could not be estimated with the same exactness. The increase of the urea is probably due simply to the drinking. Urea.

The mere passage of water through the body, whether by advancing the transitions of food or by securing the exit of the urea as such, always increases the secretion of this substance. The excess of urea, therefore, may be looked upon rather as a consequence of the disease than as connected with its origin.

In some of the instances of this disease reported by the older observers the urea has been noted as deficient; but it must be considered that before the introduction of Liebig's process there was more room for error in this respect than latterly.

In the case related at page 224, the urea was about normal in quantity; perhaps it was rather more than in proportion to the food, of which little was taken.

Uric acid on the contrary, either from its absolute deficiency or from the difficulty of collecting it from the dilute urine, usually seems to be diminished or even absent. Uric acid.

The diminution of uric acid with the increase of urea is consistent with the view that the former is convertible by oxidation into the latter.

Salts.

With regard to the inorganic constituents, they are on the whole increased. The total salts in Cox amounted to 9·05 grammes, instead of about 3, which would be due to her weight; with Botting and Russell the salts were also in excess though not so greatly.

Phosphoric acid, &c.

Looking at other observations as well as my own,[1] it may be said with general truth that the phosphoric acid generally comes to the full average of health (the case of abdominal tumour related at page 224 was an exception), while the sulphuric acid and the chlorine are increased.

I have made no separate estimations of the potash and soda, but the amount of the soluble ash shows that these are increased with their companion acids.

Earthy phosphates.

Perhaps the most striking fact after the increase of urea is that of the earthy phosphates. With the normal average of the adult at about 1 gramme, the two children Botting and Cox, neither of whom had more than one fifth of the adult weight, passed respectively ·79 and 1·25. The lime was largely increased; in the case of Botting amounting to ·176; in that of Cox varying from ·035 to ·296; quantities, except Cox's minimum, well within the adult range of health. In a case of diabetes insipidus in a man (page 224), I found that the earthy phosphates came in one day to 3·4 grammes, the lime to ·65. The magnesia is not, so far as I have seen, increased in the same proportion.

The mere increase of the drainage of the body would seem enough to cause an enhanced discharge of saline matter; the disproportionate exit of the earthy phosphates may be associated with the origin of the disease in nervous irritation, and the fact, for so it must be regarded, that in many conditions of nervous disturbance the phosphates, more particularly the calcic, are voided in abnormal quantities.

Abnormal constituents of urine.

Of abnormal urinary constituents the absence of sugar is secured by the definition involved in the term insipidus.

[1] Analyses of the urine in this disease are given by Professor Haughton, 'Dublin Quarterly Journal,' November 1863; and many are cited in Lancereaux's treatise.

Albeit the two types of diabetes are not abruptly separated ; there are many cases which existence of a trace only of sugar consigns to a border land or common territory ; while others at one period, generally the earlier, are mellitic, at another insipid.

Albumen is usually absent, though, as in the instance of Botting, it may show itself in a minute quantity, notwithstanding that there be no reasons to suspect structural disease of the kidney itself. Probably the vascular dilatation, hypothetically the mode by which the prominent symptom is produced, may facilitate the transudation of this component of the serum.

In conclusion, inosite has been detected in the urine ; but since it has been found also with diabetes mellitus, and even in health where large quantities of water have been drunk experimentally, it may be looked upon, like the saline excess, as more probably a result of the increased irrigation of the tissues, than as characteristic of the disease.

Treatment.

Chiefly by compensation.

The treatment of the disease, so far as our present knowledge goes, is rather compensatory than curative. An unlimited allowance of water will make up for the chief loss ; generous diet and medical restoratives will do the rest. And if the central lesion be not in itself dangerous the patient may by such means be kept in fair health often for many years.

Attempts to restrain diuresis useless or harmful.

Remedies designed to restrain the urinary secretion seldom fail to do harm. Opium and its alkaloids, perhaps, in the greatest measure—they disturb the digestion, make the tongue coated, and, as I have more than once seen, cause diarrhœa, while there is little counterbalancing good in diminution of urine. Belladonna and bromide of potassium are equally useless, though somewhat less injurious. Valerian, lauded by no less an authority than Trousseau, has been ineffectual in my cases; and I may say the same of camphor, which has also been commended.

Ergot, as a vascular contractor, and cantharides as a homœopathic inspiration, were, the former without result, the latter productive of increased diuresis. Arsenic I have thought useful as a tonic, but less so than iron, strychnia, and cod-liver oil. These, together with country air, plentiful food, and drink without stint, will help the patient to withstand the exhausting effects of the disease until either it subsides under the natural influences of time and change, or reaches at last its inevitable close in uræmia or advancing cerebral disease.

Tonics of use.

CHAPTER IX.

CASES OF DIABETES INSIPIDUS.

The following instances may supply some of the details wanting in the preceding account.

Case 5.

Diabetes insipidus in a tuberculous child coming on after fright. Enormous diuresis; gain of weight without eating or drinking. Disease independent of diet. Improvement when allowed to drink without restriction. Analyses of urine.

In the course of the last four years, this child, Ellen Cox by name, has been repeatedly under my care at the Hospital for Sick Children, with no advantage save that which she afforded in opportunities for observation.

She is still alive, and but for her infirmity, which now scarcely affects her general health, is so far well that she acts as a responsible and competent nurse to her smaller brothers and sisters.

She was admitted for the first time in November 1870. Until three months previously, she had been in perfect health; she then, having been a week before much frightened by an accident in which she was in danger of being set on fire, began to pass water abundantly and frequently, to drink largely, to fail in appetite, and lose flesh.

November 10, 1870.—On her admission she was 8 years of age, and weighed 21 lbs., she was small in stature, pale and emaciated, and with a peculiarly harsh and dry skin. The left apex was somewhat duller and harder than the right, and gave slight crackling sounds at the end of inspiration. Her father had had hæmoptysis, and was apparently phthisical. She felt

the cold much, often shivering. Her temperature varied but little from the normal, never below 97, or above 99. The pulse was usually quick, from 120 to 130. She frequently had headache, especially across the forehead, and sometimes felt sick. She was peculiarly somnolent, sleeping so heavily in the daytime, that she could sometimes be taken from bed, set upright, and loudly spoken to, without being awoke. Her pupils were habitually dilated, equally so.

The abdomen was examined under chloroform, but no abnormal swelling could be detected.

She had 'fancy' diet, in other words was encouraged to eat by consulting her taste; she took beer, wine, and 2 pints of milk, and was supplied with water from time to time, but was not allowed unrestricted access to it. Her sole medicine as yet consisted of cod-liver oil.

Under this regimen she passed urine in quantities which varied from 4 to 7½ pints in the twenty-four hours. It was pale and watery, with, when seen in bulk, a faint greenish tinge. It was generally nearly neutral in reaction, rapidly becoming alkaline. The specific gravity varied from 1,006 to 1,007. Beyond the aqueous excess, the only marked peculiarity was superabundance of urea. Her normal yield of urea may be taken at about 5 grammes; the quantity actually discharged when she came under observation was from 14 to 21 grammes. There was no sediment except occasionally some crystals of phosphate of lime. Details with regard to the frequent estimations of the urinary constituents are appended in a tabular form. There was never any trace of albumen or sugar.

It will be impossible to follow at length the detailed notes which bring the history of her case to the present time, November 1874. Her appetite was at first defective, and she was troublesome, peevish, and liable, on slight provocation, to violent fits of passion. She suffered continually from thirst, and was detected in the act of drinking her urine. After a time, however, March 26, 1871, she was permitted to drink water without restriction, an urn to which she could always apply being placed by her bed-side. This was followed by a marked improvement, and in fact was the only therapeutical measure from which she obtained decided advantage. Her appetite returned. The tongue, which before was often dry, kept moist. She put on flesh. Her temper mended, and she became pleasant

and good-humoured. The fashion of her countenance altered. Instead of being furrowed with wasting and misery, she assumed a look of plump content.

The fluid she drank and the urine she passed were systematically measured with the general result that on an average the two were nearly equal, excretion slightly preponderating. No allowance was made for the water involved in her solid food; this, together with absorption from the atmosphere, must have sufficed to make up the excess of the escape over the introduction of liquid.

Very little could have found its way out by any outlet but by the kidneys.

I will give the details for a few days; being on ordinary mixed diet, and allowed to drink *ad libitum*, the measurements were as follows:

	Passed.	Drank.
	c.c.	c.c.
June 11 . .	7150	5650
„ 12 . .	9250	6550
„ 13 . .	8950	7650
„ 14 . .	6950	7600
„ 15 . .	6850	8550
„ 16 . .	7980	8600
„ 17 . .	8100	6550
„ 18 . .	9250	8950
„ 19 . .	6950	5500
Daily averages .	7936	7255

These observations were made with great care, and I believe are trustworthy.

The statement that in this disease the patient gains weight without eating or drinking, apparently by the absorption of water from the atmosphere, was put to the test.

The accuracy with which so small a body could be weighed, and the closeness with which as a child she could be kept under notice, fitted her for such a purpose. On four occasions she was immediately after her dinner made to empty her bladder and thus weighed. She then was kept without eating, drinking, or passing water, and weighed when she could hold out no longer. It was always found that she had gained, though variously in amount. The results were as follows: In the first observation she gained in 3 hours, 15½ ounces; in the second, in 5 hours

and 20 minutes she gained $19\frac{3}{4}$ ounces; in the third, in $3\frac{1}{4}$ hours she gained only $\frac{1}{4}$ ounce; in the fourth she gained in $3\frac{1}{2}$ hours $3\frac{3}{4}$ ounces.

Many drugs were administered in the hope of checking the flow of urine. All were alike futile. Codeia in doses gradually increased from three quarters of a grain to 15 grains daily, caused constipation, sickness, and contraction of the pupils, but did not prevent her passing 9 pints of urine, which was about her amount without it. Opium in its totality caused diarrhœa, in other respects its action was similar to that of codeia, and belladonna, like other narcotics, had no further effect than to cause her appetite and spirits to fail, and her tongue to become coated.

Valerian, in large doses, was not attended with the beneficial results ascribed to it by Trousseau, and indeed was remarkably barren of results of any kind. Strychnia, arsenic, and iron, were each productive of some benefit of a general tonic sort, but none as touching the special disorder. Nothing lessened the urine but restricting the drink; and this was too evidently detrimental to be enforced.

She was, in company with some other patients similarly and differently affected, made the subject of a dietetic experiment, animal and vegetable food being given alternately. The details are given at page 215, diagrammatically at page 226. The changes of diet made little difference in the amount of urine; under vegetables the urea and specific gravity instantly fell, the reverse occurring with animal food.

While in the hospital, probably from the good living she enjoyed, she improved in health and gained flesh. On her first admission in November 1870, she weighed, as has been stated, 21 lbs. Before her leaving, in June 1872, she weighed 40 lbs. It was noted that her changes of diet made no appreciable difference in her appetite or weight.

The estimations of the urinary constituents made in the course of the case, with the circumstances of the patient when they were made, are stated in a tabular form.

Estimation of the Urinary Constituents in case of Ellen Cox.

Date	Quantity	Specific Gravity	Urea	Total Phosphoric Acid	Phosphoric acid with earths	Total Salts	Salts of alkalies	Salts of earths	Lime
Fancy diet, restricted drink, no medicine.									
	C.C.		grms.	grms.	grms.	grms.	grms.	grms.	grms.
1870. Nov. 18	2100	1006·7	21·0	·63	—	—	—	—	—
Fancy diet, restricted drink, Liquor Arsenicalis.									
Dec. 2	1470	1007·0	14·7	·73	—	—	—	—	—
Fancy diet, restricted drink, Arsenic and Perchloride of Iron.									
1871. Jan. 17	2210	1005·1	14·3	·55	—	—	—	—	—
Same with Opium, and Phosphoric acid drink.									
Feb. 13	2200	1006·3	23·0	1·1	—	—	—	—	—
Fancy diet, restricted drink, Cod Liver Oil and Strychnia.									
March 14	4500	1003·0	24·0	1·3	—	—	—	—	—
Fancy diet, water allowed ad libitum henceforward; Cod Liver Oil and Strychnia.									
March 28	6950	1002·5	24·0	—	—	—	—	—	—
29	4600	1002·7	20·0	—	—	—	—	—	—
30	4800	1002·5	16·0	—	—	—	—	—	—
Fancy diet; Codeia.									
May 11	5500	1002·1	16·0	—	—	—	—	—	·171
Fancy diet; Bromide of Potassium.									
July 13	5340	1002·1	26·0	1·06	·277	9·05	7·8	1·25	·296
Fancy diet; no medicine.									
Dec. 2	2330	1003·3	11·6	·58	—	—	—	—	·035
Fancy diet; no medicine.									
1872. May 13	3500	1003·5	15·7	—	—	—	—	—	—
16	3400	1003·1	13·6	—	—	—	—	—	—
Vegetable diet (Bread, Potatoes, Arrowroot, Sago, Tapioca).									
May 17	5100	1005·1	28·0	—	—	—	—	—	—
20	4000	1002·9	14·0	—	—	—	—	—	—
22	2550	1002·1	6·3	—	—	—	—	—	—
Animal (non-amylaceous) diet. Meat, Eggs, Beef-tea, Broth, Greens, Gluten Bread.									
23	5200	1003·1	15·6	—	—	—	—	—	—
24	5500	1004·3	27·5	—	—	—	—	—	—
25	5000	1005·0	30·0	—	—	—	—	—	—
26	5470	1004·9	27·0	—	—	—	—	—	—
27	5000	1004·8	30·0	—	—	—	—	—	—

Date	Quantity	Specific Gravity	Urea	Total Phosphoric Acid	Phosphoric acid with earths	Total Salts	Salts of alkalies	Salts of earths	Lime
			Vegetable diet.						
1872. May 28	5000	1004·1	20·0	—	—	—	—	—	—
29	5000	1004·2	17·5	—	—	—	—	—	—
30	5330	1003·4	18·6	—	—	—	—	—	—
31	5350	1002·7	18·7	—	—	—	—	—	—
June 1	6500	1002·4	16·2	—	—	—	—	—	—
2	6000	1002·9	18·0	—	—	—	—	—	—
3	5150	1002·9	18·0	—	—	—	—	—	—
4	5350	1002·0	16·0	—	—	—	—	—	—
			Animal (non-amylaceous) diet.						
5	5000	1003·7	20·0	—	—	—	—	—	—
6	4300	1004·6	17·2	—	—	—	—	—	—
7	4700	1004·2	23·7	—	—	—	—	—	—
8	5550	1003·6	22·2	—	—	—	—	—	—
9	4750	1004·1	19·0	—	—	—	—	—	—

Comments. The diuresis, amounting as it frequently did to a third of the weight of the body in 24 hours, was such as almost never occurs excepting with diabetes of the insipid variety.

The child was clearly tuberculous, a condition which has been discovered in other cases of the same sort; she had likewise been exposed to fright, which though a cause of saccharine diabetes, is not recognised with regard to the variety which existed in this instance.

This child, like others suffering in like manner, was influenced only injuriously by measures designed to lessen the secretions; this held as touching narcotics and even more obviously with the restriction of drink. The vice of the disease is in the exit, not in the introduction of water; it is polyuria not polydipsia: the patient does not urinate overmuch because he so drinks; but he so drinks to restore the loss occasioned by the excessive urination. Hence if drink be insufficient deterioration of health follows, which must be attributed to dehydration of blood and tissue; and the blood unable to restore itself by the natural channel will absorb, though scantly and ineffectively from the atmosphere.

Good living and general restorative treatment bore their fruit in nearly doubling the weight of the child between the ages of 8 and 10. Special measures were, as has been seen, at best useless.

The peculiarities of the urine may be briefly summed up as excess of water and consequent excess of some other ingredients, in particular of urea.

Case 6.

Diabetes insipidus in a child; daily urine exceeding half the weight of the body; analyses of urine; few symptoms beyond a general condition of feeble health; effects of diet; inutility of medicinal treatment.

Julia Botting, a thin child, with light hair, a pink face, and rickety chest, born of healthy parents, had good health until she was $2\frac{1}{2}$ years old. She then, without assignable cause, began to pass water and drink in unusual quantities, which increased until her admission into the Hospital for Sick Children, a year later.

May 18, 1871.—She then was lively and bright, and setting aside her special symptoms, thirst and diuresis, would have been regarded as well. The thoracic sounds were those of health; no organ within the abdomen was tangibly enlarged; the bowels, appetite, pulse, and temperature, were natural.

She weighed 23 lbs.

The interest pertaining to her case caused her to be frequently an inmate of the hospital, where, indeed, she now is (June 1874).

She was fed liberally and variously, and allowed to drink water without restriction. But she did not respond to the good living as did her companion, whose case has been just related, but for many months either remained stationary in weight or lost, insomuch, that on June 26, 1873, when about to leave the hospital, she weighed only 22 lbs., one pound less than on her first admission, more than two years previously. At present (June 1874) she weighs 27 lbs., her age being 6 years.

The diuresis fluctuated. It was greatest in cold weather; and the child was then in all respects worse; she shrivelled and

became fretful with cold, expanding and becoming exhilarated with warmth.

The urine at its maximum, which it attained during the autumnal cold of 1871, ranged during three weeks from 6,000 to 7,600 c.c., or from 13 to 17 wine pints or pounds.

She at this time weighed 23 lbs., her daily urine constantly exceeded half, and at least on one occasion, exceeded two thirds of the weight of her body.

She always drank rather more liquid than she passed urine.

The specific gravity of the urine touched a lower point than I have known to be reached in any other instance. It was often below 1,002. To guard against error, once when my weighing had given a specific gravity of 1,001·8, I asked Dr. Noad, in whose researches the accurate determination of the specific gravity bore a part, to repeat the observation with his own instruments. With adjusted temperature and all precautions, the specific gravity was 1,001·7.

The urine was pale and clear generally, when seen in bulk with a faint greenish tint. It was sometimes faintly acid, at other times neutral or alkaline from fixed alkali. It soon became ammoniacal. A faint cloud of albumen was sometimes but not always to be detected by nitric acid. The microscope showed only occasional crystals of triple phosphate and scales of squamous epithelium. The following table gives the several estimations of the urinary constituents which were made. The leading peculiarities were as in the case of Cox, excess of water and urea. Her normal yield of urea would be about 5 grammes. On mixed diet, it is shown by the table to have ranged from 9 grammes to 23 grammes. Vegetable diet reduced it to a minimum of 6·7. Under animal diet it reached a maximum of 24·0.

Estimation of Urinary Constituents in case of Julia Botting.

Date	Quantity	Specific Gravity	Urea	Total Phosphoric Acid	Phosphoric acid with earths	Total Salts	Salts of alkalies	Salts of earths	Lime (CaO)	Magnesia (2MgO)
Mixed diet and valerian, water ad libitum throughout.										
	C.C.		grms	grms.	grms.	grms.	grms.	grms.	grms.	grms.
1871. May 30	3300	1003·6	14·0.	·6	—	—	—	—	—	—
Mixed diet, no medicine.										
Nov. 15	7650	1001·8	23	·57	·311	5·60	4·81	·79	·176A	·068A
Mixed diet, no medicine.										
1873. May 13 Body weight = 24½ lbs.	1925	1004·2	9·6	—	—	—	—	—	—	—
16 Wgt = 24½ lbs	2050	1005·3	10·2	—	—	—	—	—	—	—
Vegetable diet (Bread, Potatoes, Arrowroot, Sago, Tapioca, Rice).										
May 17 Wgt = 24 lbs	2000	1003·8	11·0	—	—	—	—	—	—	—
20	2280	1002·1	9·1	—	—	—	—	—	—	—
21	2000	1002·6	9·0	—	—	—	—	—	—	—
22 Wgt = 24 lbs	2745	1002·2	9·6	—	—	—	—	—	—	—
Animal diet (Meat, Eggs, Broth, Beef-tea, Greens, Gluten Bread).										
May 23	2500	1003·3	12·5	—	—	—	—	—	—	—
24	2000	1005·6	16·0	—	—	—	—	—	—	—
25	3125	1005·7	24·0	—	—	—	—	—	—	—
26 Wgt = 22¾ lbs	2700	1005·5	21·0	—	—	—	—	—	—	—
27	3000	1005·1	19·5	—	—	—	—	—	—	—
Vegetable diet.										
28	2000	1002·8	8	—	—	—	—	—	—	—
29 Wgt = 22¼ lbs	2160	1003·0	8·6	—	—	—	—	—	—	—
30	1500	1003·4	6·7	—	—	—	—	—	—	—
31	2250	1002·2	6·7	—	—	—	—	—	—	—
June 1	3000	1002·2	7·5	—	—	—	—	—	—	—
	3500	1002·5	9·5	—	—	—	—	—	—	—
	2900	1001·8	10·1	—	—	—	—	—	—	—
4 Wgt = 21¾ lbs	3000	1001·7?	9·0	—	—	—	—	—	—	—
Animal diet.										
5	2800	1003·4	12·6	—	—	—	—	—	—	—
6	3000	1003·4	15·0	—	—	—	—	—	—	—
7	3160	1002·2	14·2	—	—	—	—	—	—	—
8	4000	1002·5	20·0	—	—	—	—	—	—	—
9	3700	1001·9	14·8	—	—	—	—	—	—	—

A dietetic experiment was made parallel to that to which Ellen Cox was subjected. It was shown that the urine was not increased by an amylaceous diet, while the urea was at once lessened. Under this diet she throve, while under animal food she lost weight and suffered in health.

For the space of a fortnight the total of the fluids drunk was carefully measured against the urine. Although on one or two days the urine out-measured the drink, the average was the other way. Besides the water taken as drink, it is obvious that a small portion was introduced in the solids, of which this statement gives no account.

	Drink	Urine
	c.c.	c.c.
1874. May 28	6600	5250
29	5750	5250
30	5300	4500
31	5100	5300
June 1	4250	4500
2	5250	5100
3	6150	5100
4	6100	5250
5	6100	5150
6	6300	6100
7	6250	5100
8	6150	5500
9	6250	5500
10	6300	5600
Fortnight's average	5848	5228

No drugs lessened the diuresis. So little did opium, as tincture, appear to control the secretion, that it was under this remedy, together with cold weather, that the urine reached its maximum of 17 pints. The use of this medicine was accompanied with diarrhœa, and much disturbance of temper and general health.

Ergot given in view of its reputed action upon the blood-vessels, produced no recognisable effect. Valerian, camphor, and bromide of potassium, were equally without result as far as the special symptom was concerned; and cantharides, which I was asked to try on the principle, I suppose, of *similia similibus*, was followed, as might have been anticipated, by its aggravation. Cod-liver oil and tonics resorted to, when, to her obvious

advantage, special treatment had been discontinued, improved her general condition.

She varied but little from year to year. She, however, did not gain weight in proportion to her age and increasing stature, acquiring only 4 pounds in as many years, and exchanging her plump cheeks and pink colour for a somewhat worn and pallid look.

Once, at the Convalescent Home at Highgate, which is colder than the parent establishment, she became slightly jaundiced and had œdema of the legs.

At the present time (June 1874) she passes from 5000 c.c. to 6100 c.c. of urine, and is, save in the respects which have been mentioned, much as when she first came under notice. She is not drowsy or sluggish. Her intelligence is fully that belonging to her years. She has no evidence of disease of the nervous centres or of tubercle. Her appetite is fair. Her temperature ranges from 97 to 99.

This case appears to be one of much severity, whether looking at the quantity of urine in relation to the size of the child, or to her increasing enfeeblement and attenuation under the disorder. It can scarcely be expected but that she will eventually succumb to its direct or indirect effects. The end may probably be retarded by judicious support, dietetic and medicinal; but the attempts made to that end, as in every other case I have seen, lent but little encouragement to the use of measures designed to lessen the diuresis.

Case 7.

Diabetes insipidus, beginning at the age of 12 months, without ostensible cause; intercurrent attack of scarlatina, the diuresis persisting throughout.

Percy Russell, a boy living at Malvern, belonging to a healthy family save that one of his brothers had had fits, as also had he himself once with chicken pox, and again with what was termed inflammation of the lungs, became at the age of 12 months, without ostensible cause, the subject of inordinate thirst and diuresis.

He had been brought up by hand on milk and farinaceous food.

The thirst was such that he would seize and swallow any liquid within his reach; he once thus drank undiluted brandy, at another time parafin oil, and his urine habitually.

A large quantity of pale urine was passed during the day at intervals of from a quarter of an hour to an hour, and every night he made his bed to swim.

His appetite was ravenous; he was fed chiefly on farinaceous food and skim milk, and lost neither substance, colour, or strength.

So far went the report of the parents, adding that his urine had been examined by a chemist (whom, considering the improbability of his conclusion, I ventured to interpret as not a chemist, but a druggist) and found to contain sugar.

He was sent to the Hospital for Sick Children in London in May 1874, he then being 2 years and 3 months old, having had the disorder for 15 months.

He was plump, sturdy, and full of activity and vigour. Setting aside his speciality, the manufacture of urine, he presented a type of robust health.

No evidence could be found of tubercular or other organic disease. The chest was well shaped and amply resonant; a few sounds of bronchial sibilus were found in the right apex and the left base; but these proved transient.

The abdomen was examined under chloroform; no tumour or enlargement could be felt in the region of the kidneys or elsewhere.

The pulse was that of health; the tongue clean and not dry; the skin soft and naturally moist; the bowels open daily. The temperature, excepting when exalted by scarlatina, ranged from 97 to 98.

Until he caught this disease his health was good, excepting that on one or two occasions he had small boils or superficial abscesses; and was subject to a slight eruption of a vesicular or pustular character which might be looked upon as a diminutive of either chicken pox or impetigo.

The urine was clear and of a pale greenish tint; it was always faintly acid or neutral, rapidly becoming fishy and ammoniacal. It contained no trace of either albumen or sugar; nor could anything abnormal be discovered with the microscope.

Collected for 24 hours ending on May 29, 1530 c.c. were obtained, reckoned to be about half of what he passed. Within the same space he had drunk 3110 c.c. The quantity obtained, which had a specific gravity of 1003·1, gave the following amounts, which may fairly be taken at half the total for the 24 hours :—

Urea	9·1 grammes
Uric acid	none separable
Phosphoric Acid	·61 grammes
Chlorine	1·35 ,,
Sulphuric Acid	1·23 ,,
Alkaline Salts	3·25 ,,
Earthy Salts	·248 ,,
Lime	·039 ,,
Magnesia	·018 ,,

With regard to the quantities drunk and passed, the following observations were made; some of the urine, however, was always lost, so that the figures in this respect never represent the whole.

From June 9 to 18, daily drink varied from 3000 c.c. to 5100 c.c.; his collected urine from 2000 c.c. to 3300 c.c. His weight being 25½ lbs. his daily urine could not be estimated at less than a quarter of his weight.

On June 18 he showed the initiatory symptoms of scarlatina and passed in due course through a well-marked but uncomplicated attack.

Unlike, however, many cases on record, the exanthem scarcely modified the flux even temporarily, leaving it precisely as before.

From June 19, when the disease began with a temperature of 102·5 to July 12, when the boy left the hospital convalescent, the drink varied from 3465 c.c. to 5550 : the collected urine from 2650 c.c. to 3900 ; the diuresis persisting with little change, the thirst apparently somewhat increased. It must be observed that while in bed with this intercurrent disease the urine was collected with little loss.

Case 8.

Diabetes insipidus associated with an abdominal tumour, pain in the lower spinal and iliac regions, with subsequent symptoms indicative of hepatic disease. Cancer of the liver, as ascertained by post-mortem ex-

amination, with secondary tumours in the position of the solar plexus, many of the branches of which were involved in the growth.

Mr. Y——s, a stout man of the age of 60, with a complexion suggestive of malignant disease, came to me on January 15, 1874, with, as was supposed, diabetes. It was at once ascertained, however, that the disorder was not of the mellitic sort, for some urine which he was able to produce was of low specific gravity and contained no trace of sugar.

He had been of temperate habits, and had had good health until six months previously, when he began to lose appetite and bulk. Four months later, he began to suffer from thirst and dryness of the mouth, with profuse diuresis; and at the same time he began to have pain in the back limited to the left side, extending from the lower renal region to the lower gluteal, having its greatest intensity about the posterior spine of the ilium and the adjoining part of the left crest.

This pain when I saw him was his chief source of complaint; it was not increased by pressure but much by movement, upon which it became shooting and severe, whereas when at rest it was slight, or even at times absent. Though reaching the lowest part of the left gluteal region it never entered the thigh.

Examining the abdomen, I found, what the patient himself was not aware of, a rounded hard tumour, which felt like an orange, immediately behind the abdominal wall just under the ensiform cartilage. Tracing its connections, it proved to be only the most superficial part of a large mass which lay deeply in the right hypochondrium, reaching from the ribs to the level of the umbilicus, and from three inches to the left of the median line across the front and right side of the belly deeply into the right loin, where it was lost behind the lumbar muscles. This was nowhere superficial except at the nodule under the sternum, being everywhere else overlaid by bowels, as declared by their resonance, and for the most part somewhat obscurely felt behind them.

It was not possible to doubt that the tumour was malignant, and in the presence of such a growth and of the obstinate and severe lumbar pains, and in the want of any other circumstance to account for it, that the polyuria was due to the implication of some portion of the abdominal sympathetic in relation to the

kidneys. The organ primarily the seat of the growth was less clear; though in exactly the position of the liver it was covered by bowel to an extent rare with hepatic tumours; there had been as yet no disturbance in jaundice or ascites of hepatic function, and the deep lumbar pain was suggestive at least of the association of structures behind the liver with the growth which occupied its position.

The tongue was red, dry, and glazed; the appetite wanting; his thirst compelled him to be continually drinking water both day and night; he passed urine about every hour during the night, somewhat less often in the day, about half a pint each time, clear and pale.

Collected for 24 hours it amounted on January 15 to 5650 c.c., or about ten imperial pints, and gave the following results:

Sp. gr. 1004·9
Urea 33·9 grammes
Phosphoric acid 1·1
Salts of the alkalies 11·2
Salts of the earths 3·4
Lime ·651
Magnesia ·137

Such palliation as was possible was accomplished by means of small opiates, subcutaneously and otherwise, but the hypochondriac tumour slowly increased, while the lumbar pain extended from the left side, to which it had at first been confined, to the right side and the region of the hips, being always aggravated by movement, sometimes to an excruciating degree. Then he became jaundiced, but not deeply, the bowels became constipated and the motions wanting in bile, and fluid accumulated in the abdomen; symptoms which sufficiently pointed to what at first had been doubtful—the hepatic seat of tumour.

Dyspnœa from abdominal distension called for the use of the aspirator, and the withdrawal by its means of a pailful of ascitic fluid. After a long course of severe suffering, he gradually sank and died on December 24, 1874. The character of the urine remained with little variation throughout, save that towards the last it displayed a trace of albumen. The quantity was generally about what has been stated; the specific gravity usually about 1004.

Through Mr. Fuller, under whose care he usually was, and with whom I had occasionally seen him, I obtained permission to examine the body.

The brain was full of blood, but there were no regions of porosity nor any other evidences of disease appreciable to the naked eye. Sections were prepared and examined microscopically in the manner practised in all the instances of diabetes mellitus which have been described. Many of the larger vessels, chiefly the veins, were full of blood, this condition being general throughout the parts examined, and common indeed, as was evident without the microscope, to the whole brain; but none of the blood had found its way to the outside of the distended vessels, nor were there seen any perivascular erosions, or any products of nervous decay, or signs of destruction of tissue. The congestion was clearly accidental rather than essential, connected more probably with the mode of death or later circumstances of the illness than in any direct manner with the polyuria.

The tumour which had been felt during life proved to be the liver, enormously enlarged, so as to reach below the umbilicus, and transformed in a manner at first sight like that belonging to some forms of cirrhosis, being covered with deeply divided bosses like half oranges, while the whole organ was rounded so as to approach a spheroidal shape, and its surface covered with irregularly thickened capsule. On section more than two-thirds of its bulk proved to consist of confluent masses of hard encephaloid growth, many of which in their centres had become gritty from degenerative change.

The growth had extended backwards along the line of the hepatic artery, but external to its wall, in several separate nodules which lay in the small omentum and in the areolar tissue between the peritoneum and the aorta, apparently in the place of lymphatic glands. These nodules were of similar material to the growth in the liver, but softer and evidently more recent. The largest of them lay about the cœliac axis; a long winding process almost wholly encircled the vessel, though not closely, while the bulk of the mass lay at its end in the interval formed by the divergence of the hepatic and splenic arteries, and between the cœliac axis and the superior mesenteric artery. A part of the same growth had thrust itself between the portal vein and the vena cava, lying in contact with both. The body of the mass, between the hepatic and splenic arteries, was of an ovoid shape, and measured about an inch and a half in its longer, an inch in its shorter diameter. Several other similar,

but somewhat smaller growths were disposed in the post peritoneal cellular tissue about the pancreas, the right supra-renal capsule, and the right renal artery. All were thinly surrounded with inflammatory induration, together with which the cancerous nodules formed a bulky and prominent mass between the aorta and the posterior wall of the peritoneum, and mostly between the cœliac axis and the superior mesenteric artery.

The semilunar ganglia, the solar and renal plexuses were all in close relation to the mass of cancer; they were dissected out with much care by my clinical clerk, Mr. F. M. Hawkins. The semilunar ganglia and renal plexuses though close to the mass were not adherent to, or obviously compressed, by it. Much of the solar plexus was intimately involved in it; many of its branches were traced to its surface, and there lost in the adhesions by which it was surrounded.

The kidneys were about of natural size, but they were highly and minutely injected, the interlobular capillaries being everywhere morbidly distinct. The examination of hardened sections of these organs with the microscope showed no further change than a somewhat excessive and irregular growth of epithelium in the tubes.

The colon was remarkably distended throughout (from paralysing pressure upon its nerves?), and was full of lumps of fæces.

Comments.

The point of interest in this case is the origin of the polyuria in pressure upon the abdominal sympathetic; a fact to which the circumstances of the case pointed in a manner which was clearly recognised during life and which was instructively explained by subsequent dissection.

The obvious disturbances early produced by the growths behind the peritoneum, closely related as they were to important nervous structures, was in striking contrast with the insidious and long latent course of the parent formation in the liver. The first definite symptoms, polyuria and pain in the back, were wholly attributable to the secondary tumours; at this time the hepatic mass was palpable and must have been long existent though undiscovered. The origin of secondary growths from hepatic cancer, arranged as in this case along the lymphatics which travel with the hepatic artery, is rare. Hepatic cancer is

generally itself secondary, and is usually too quickly followed by death for the development of tumours secondary to itself.

In this instance the solar plexus was extensively involved in the disease; many of its fibres were, as has been stated, inseparable from the growth; and it can scarcely be doubted that the renal hyperæmia and the diuresis were both due to the influence thus wrought upon nerves immediately connected with those of the kidney.

I am not aware of any other instance of polyuria in the human subject in which the symptom has been thus definitely traced to pressure upon abdominal nerves, though the coincidence of abdominal tumours with the symptom has, as in the example at page 190, led to the inference that some such condition existed.

CHAPTER X.

THE EFFECTS OF DIET IN DIABETES INSIPIDUS, CONTRASTED WITH THOSE IN DIABETES MELLITUS.

Does the difference between insipid and saccharine diabetes depend on age only?

THE prevalence of the insipid nearly to the exclusion of the saccharine diabetes in early childhood, causes one to ask how far this may be due, not so much to a real inequality of distribution, connected with differences in the nature and proclivity of the two diseases, as to a possibility that with one and the same pathological change the symptoms may be determined as insipid or mellitic by the age and circumstances of the subject. Supposing that sugar in both cases is poured in excess into the blood, is it in childhood withheld from the urine by the active demands of growth and development?

The tissues need more sugar in childhood than when structure is complete, as witnessed by the love of children for sweets; is it possible that in early life these eager tissues consume the sugar which, at a later period, is left to be discharged by the kidneys? Since the use of the tissues for sugar must be limited, we can find an answer to the question in the effects of food. The sugar of diabetes mellitus is increased by the ingestion of starch; is it possible in diabetes insipidus, by urging an amylaceous dietary, to increase the making of sugar beyond its possible consumption, and so make the disorder mellitic? The answer is negative; and in conclusion the disorders essentially different. Starch in the mellitic disorder is totally, or in certain proportions, ejected as sugar, to the injury of the patient; while with the insipid,

Can diet make the insipid mellitic?

it is not possible to give enough starch to make the urine saccharine, or too much to be naturally assimilated.

Dietetic experiments.

Two typical subjects of insipid diabetes, who were together in the hospital, were fed as exclusively as might be, upon starch, that diet being abruptly alternated with one as purely nitrogenous.

The urine was collected for each 24 hours, and examined as to quantity, specific gravity, sugar, and urea. For comparison, like observations were afterwards made upon two cases of saccharine diabetes, which were together subjected to similar alternations of diet. The results obtained in each pair of cases are here given diagrammatically, and elsewhere in figures, which are more minutely true.

Their results.

The general results may be briefly stated. In the insipid cases, starch failed to develop any trace of sugar, or to increase in any marked manner the quantity of the urine. With the saccharine, starch increased as usual both the sugar and the amount. With the insipid, vegetables caused an immediate diminution in the discharge of urea; whereas with the saccharine, the first effect of a non-nitrogenous diet was to increase the excretion of this nitrogenous compound—a striking result, which I have noticed in other instances. It appears to depend on the increased discharge of water which for a time takes with it a corresponding excess of urea, notwithstanding that less of its material is introduced. The excess thus produced is not long maintained, but after a few days is exchanged for a deficiency.

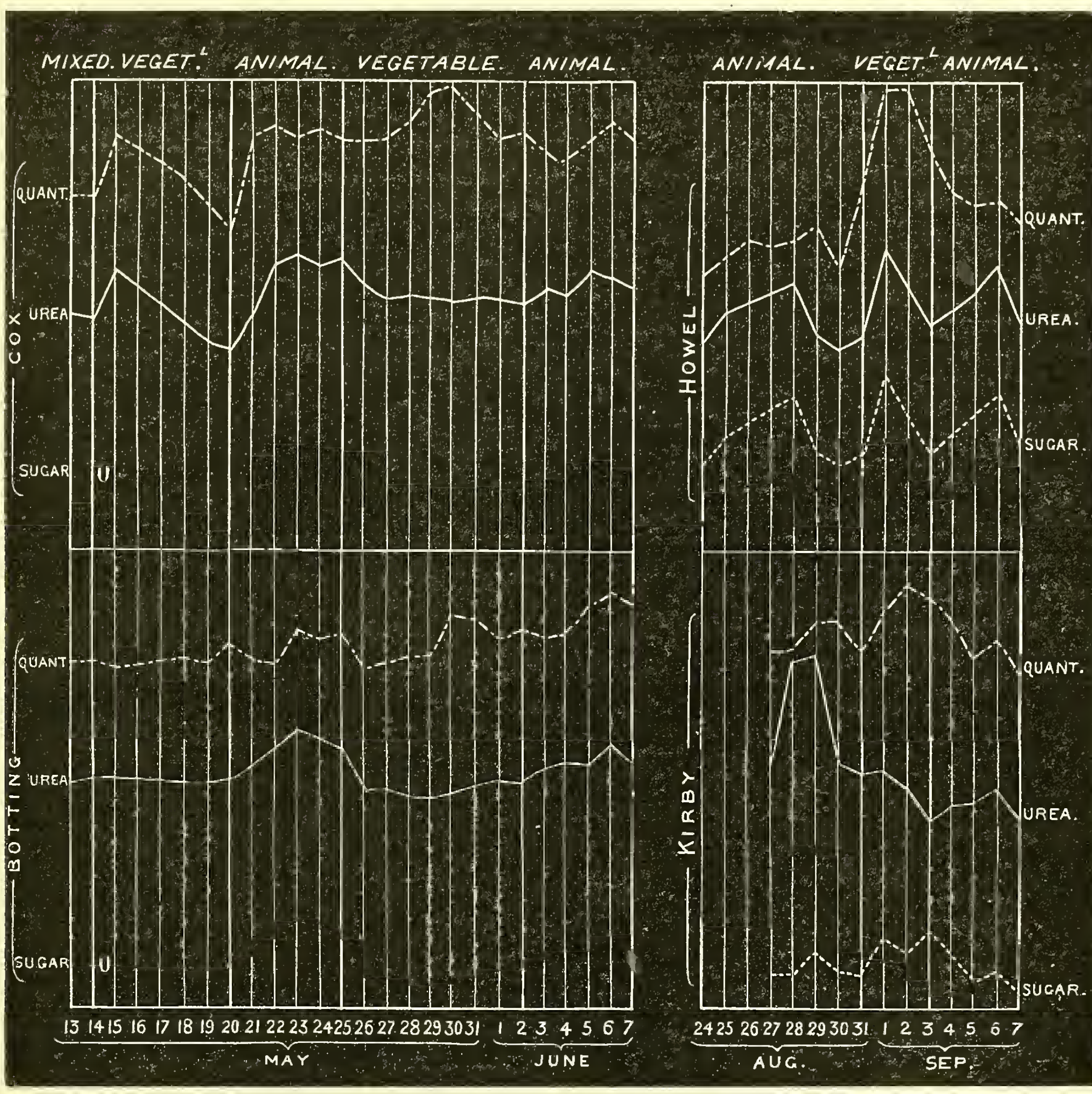
The tendency which the urea has to vary with the excretion of water, even more immediately than with the nature of the food, is shown by the general parallelism of the lines of urea and quantity.

As contrasting the effects of diet in the two forms of diabetes, it may be stated that the vegetable diet agreed much better with the insipid subjects than the meat diet; they ate it with appetite, gained weight, and improved in appearance. Under meat, Botting especially did badly;

lost weight and became more thirsty. It is scarcely necessary to add that with the mellitic patients the reverse was observed, increase of thirst and exaggeration of symptoms ensuing from the vegetable regimen.

Effects of animal and vegetable diet upon the urine in two cases of diabetes insipidus, contrasted with that in two cases of diabetes mellitus.

DIABETES INSIPIDUS. DIABETES MELLITUS.



Vegetable diet = Bread, potatoes, arrowroot, rice, sago, tapioca.
Animal diet = Meat, beef-tea, broth, eggs, green vegetables, gluten bread and gluten flour.
Water ad libitum, and half a pint of milk daily, were given throughout.

For numerical details in case of Cox see p. 215; in case of Botting p. 219; in case of Howel, p. 177; in case of Kirby p. 163.

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